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HEART MURMURS

PART I

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Auscultation of the heart, depending as it does on the acuity of the auditory sense and providing information commensurate with the observer's experience, cannot always determine unequivocally the various sound effects that may take place during systole and diastole   It is not surprising, therefore, that auscultation tied to traditional theories may sometimes lead to a wrong interpretation of the condition, although a judgment born of ripe experience in clinical medicine and pathology will avoid serious mistakes   It is more than fortuitous that modern auscultation has grown on such a secure foundation, but it is imperative that for the solution of outstanding problems there should be precise means of registering heart sounds   This is why a phonocardiogram was included in the examination of a series of patients presenting murmurs

As each patient attended for the test, the signs elicited on clinical auscultation were first noted and an opinion was formed on their significance   Cardioscopy was invariably carried out, and, when necessary, teleradiograms were taken,   Limb and chest lead electrocardiograms were frequently recorded in addition to the lead selected as a control for the phonocardiogram   Many cases came to necropsy   The simultaneous electrocardiogram and sound record was taken by a double string galvanometer supplied by the Cambridge Instrument Company, and the length of the connecting tube leading from the chest to the amplifier was 46 cm   Although the amplitude of sounds and murmurs was matched against each other in individual patients, there was no attempt to standardize the intensity of murmurs in terms of amplitude in different patients,   in fact it was varied deliberately in order to produce such excursion of the recording fibre as would best show the murmur

The actual place of the murmur in the cardiac cycle received first attention, and its intensity was only incidentally observed and noted   Before engaging in a phonocardiographic analysis of heart murmurs it is necessary to know the place occupied by each heart sound in the cardiac cycle as timed by the simultaneous electrocardiogram   In the physiological tracing obtained with a short connecting tube of 46 cm the auricular moiety of the first heart sound begins at the end of the P wave of the electrocardiogram, occasionally it starts a little later, but never earlier   During the R–S period the auricular sound is reinforced abruptly by the ventricular moiety of the first heart sound   This combined sound effect is completed as a rule before the start of the T wave, at the end of the T wave the second heart sound starts (Fig 1)   After a brief interval the third heart sound is usually seen, and it is often obvious though inaudible on auscultation

To simplify the location of murmurs in relation to the separate phases of the cardiac cycle it is well to draw a line through a point that marks the end of the S wave of the electro- cardiogram and prolong it to intersect the phonocardiogram   this may be named the S line A murmur that precedes the S line is the effect of auricular systole, if it starts at the S line
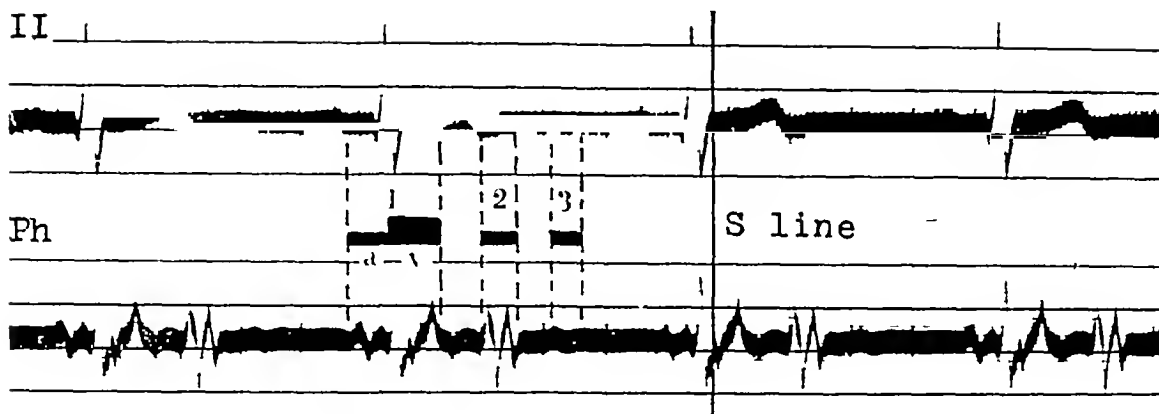
FIG 1 —Normal phonocardiogram showing the heart sounds in relation to the electrocardiogram The S line drawn at the end of the S wave of the electrocardiogram and continued to intersect the phonocardiogram, marks the early phase of ventricular contraction The auricular (a) and ventricular (v) moieties of the first heart sound are shown, as well as the second (2) and third (3) heart sounds, the third was inaudible

it coincides with the early phase of ventricular systole, if it starts a little later than the S line the murmur occupies mid-systole Next the customary form of the graphic complex depicting the separate normal heart sounds should be studied in order that the variant produced by the addition of a murmur may be recognized They differ one from the other only in the frequency of the vibration which creates them Thus, the oscillations produced by a heart sound are fewer or coarser, those produced by a murmur are more numerous and finer—they bear the same relation to one another as the teeth of a coarse hair comb bears to a fine one (Fig 2)
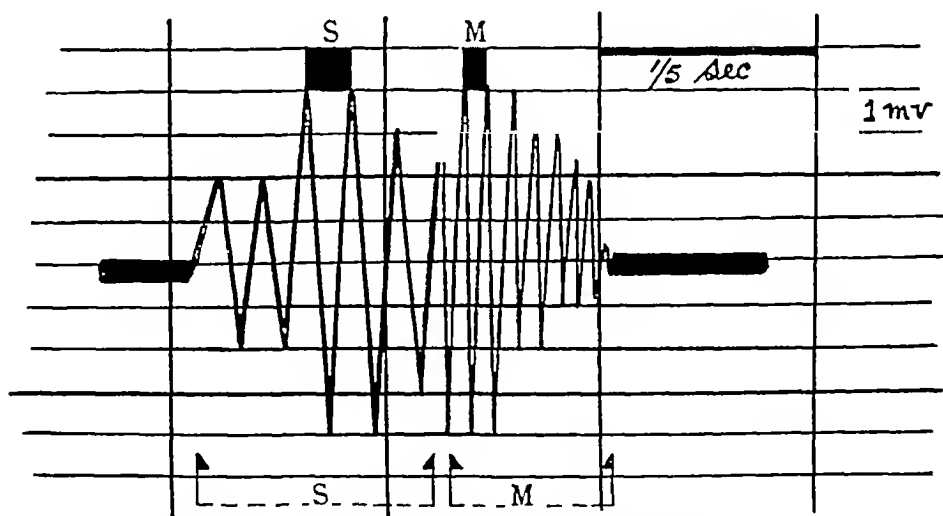
FIG 2 —Diagrammatic representation of a heart sound (S) and murmur (M) in the phonocardiogram The sound is a coarser vibration than the murmur, and the distance between each vibration forms a square in relation to the millimetre scale in the case of a heart sound and an oblong in the case of a murmur

A phonocardiographic study of murmurs is fruitless unless it is closely linked with the clinical analysis of the patients concerned The findings of this investigation, therefore, are discussed in relation to patients in seven main clinical groups, namely, healthy subjects, mitral valve disease, aortic valve disease, hypertension, congenital heart disease, heart block, and anæmia

I THE INNOCENT MURMURS

It has been traditional to speak of functional murmurs in the mitral area, but a search of the literature has shown a scarcity of observations on the characteristic features, apart from their quiet quality, that might identify such murmurs as the innocent kind   The need for such observations becomes obvious when clinical cardiology includes within its scope the examination of school-children whose playtime activities have been restricted and their early schooling neglected by non-attendance, recruits who have been denied military service and relegated to a low health category by medical boards, applicants for life insurance either rejected or accepted at increased premiums, and casual patients whose past health history recounts the handicap from restrictions imposed after examination of the heart—all because an insignificant murmur had been mistaken for one that indicates organic heart disease   Should this murmur be associated with " growing pains " or with a past history of rheumatic fever, the unjustified invalidism is more certain to be enforced   This uncertainty regarding individual mitral murmurs has imparted to them an ambiguity that has greatly hindered the diagnosis of cardiovascular disorders   It is clear, therefore, that identification of the *innocent* murmur, is as important, if not more important than the recognition of a murmur signifying disease and requires such specific clinical and graphic features as will make its diagnosis easier and surer

Among patients attending the Cardiac Department of the London Hospital during four years there were 330 with an innocent mitral murmur   Care was taken to establish its benign nature, but naturally short of necropsy   A routine clinical examination followed a medical history, and special attention was paid to the site, intensity, length, and conduction of the murmur, and the effect of posture, respiration, and tachycardia upon it   Its position in the cardiac cycle, often difficult, was particularly sought, and the presence of a thrill was always tested   Diastolic murmurs were never present   An electrocardiogram was often taken whenever it might help to exclude certain organic disease, but as it never showed changes peculiar to the innocent group, it was not adopted as a routine   A selected lead was, of course, recorded to control the phonocardiogram whenever this was taken   Great reliance was placed on cardioscopy, which was used in every case and the progress of a barium swallow was watched in both oblique positions   Phonocardiography was applied frequently and as the investigation proceeded the features of the tracing could be predicted after clinical examination, such sound records were compared with those obtained from the mitral area in patients with heart disease

Following the clinical and phonocardiographic examination it was found that although subjects with innocent murmurs could be conveniently separated into certain groups, the exact mechanism of the murmur could not be determined as neither the clinical nor the special examination provided a clue   The condition of the pericardium, mediastinum, lungs, pleura, and diaphragm was scrutinized during radiology of the chest, but this showed no obvious or consistent abnormality and failed to explain the source of the murmur   Even phonocardiography, which demonstrated the place of the murmur in relation to the cardiac cycle, did not disclose the mechanism   Necropsy in these subjects is awaited, although such an event would naturally be fortuitous, even then it is unlikely that the cause of the murmur would show   The fact that the mechanism of the innocent murmur is unexplained need not encourage conjecture on its ways of production, and must not delay the building of a clinical syndrome that might by itself decide the innocent nature of the murmur   Although the first grouping was on clinical grounds, phonocardiography later showed that these grounds were valid, hence great emphasis is given to sound records in this investigation

The Murmurs in Mid-Systole

This was by far the commonest variety of innocent murmur and accounted for 262 of the 330 cases   It occurred with equal frequency in both sexes   The murmur was never rough nor harsh, but it could be described as roughish or blowing in character, very occasionally it was musical   The distinctive feature was the position of the murmur in mid-systole so that in the phonocardiogram (Fig 3 and 4) it commenced a little way beyond the *S line* and did not last long   In this respect the tracing differed from the one obtained in mitral disease, where the murmur usually preceded the S line, starting within the P–R period (Fig 5)   Although

Fig 3 —The innocent systolic murmur of reclining posture   In this and succeeding records the murmur is indicated by a black line, the start and finish of which is projected on to the electrocardiogram and phonocardiogram
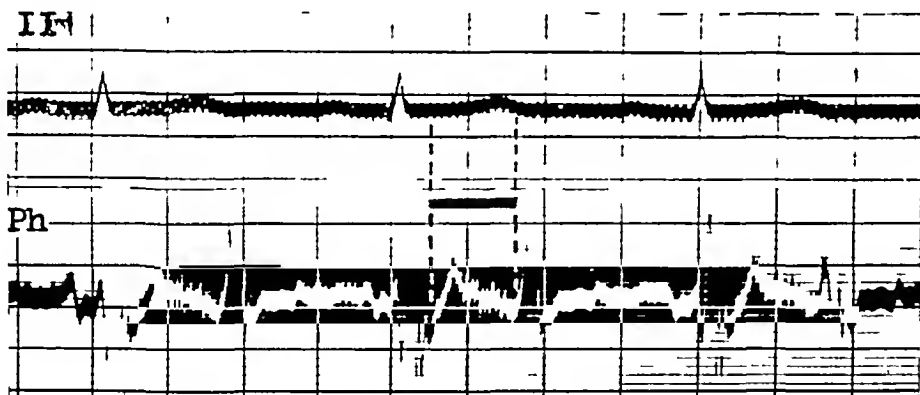
Fig 4 —The innocent systolic murmur of upright posture

it was not always possible, especially under the handicap of tachycardia, to establish the mid-systolic position of this murmur by auscultation, whenever a gap was detected between the first heart sound and the murmur following it, it was proof of its innocence   The corroborative test of phonocardiography, therefore, has been invaluable in establishing the validity of the clinical signs proposed for the identification of the separate varieties of innocent murmur

Apart from its selective position in systole—slightly postponed in fact—which gives to this murmur its distinctive character, there were clinical features that decided by themselves its innocent nature even without a phonocardiogram   From a consideration of the site and intensity of the murmur, and the influence upon it of posture, it was found that the cases

Murmurs (early systolic) of mitral stenosis		Innocent murmurs	
The "presystolic" murmur	The "systolic" murmur	Mid-systolic	Late systolic
41	52	17 L	27
35	17	13 L	14
18	18	14 R	54
46	17	28 U	41
32	12	13 R	7
32	55	29 R	44
38	54	17 R	22
39	48	18 R	51
27	39	12 L	7
38	63	15 L	20
33	57	11 L	39
38	42	15 L	52
27	35	9 L	15
13	32	21 L	46
50	28	18 R	12
44	31	30 L	33
28	36	17 R	20
19	14	19 U	47
34	23	11 R	38
37	60	18 U	18
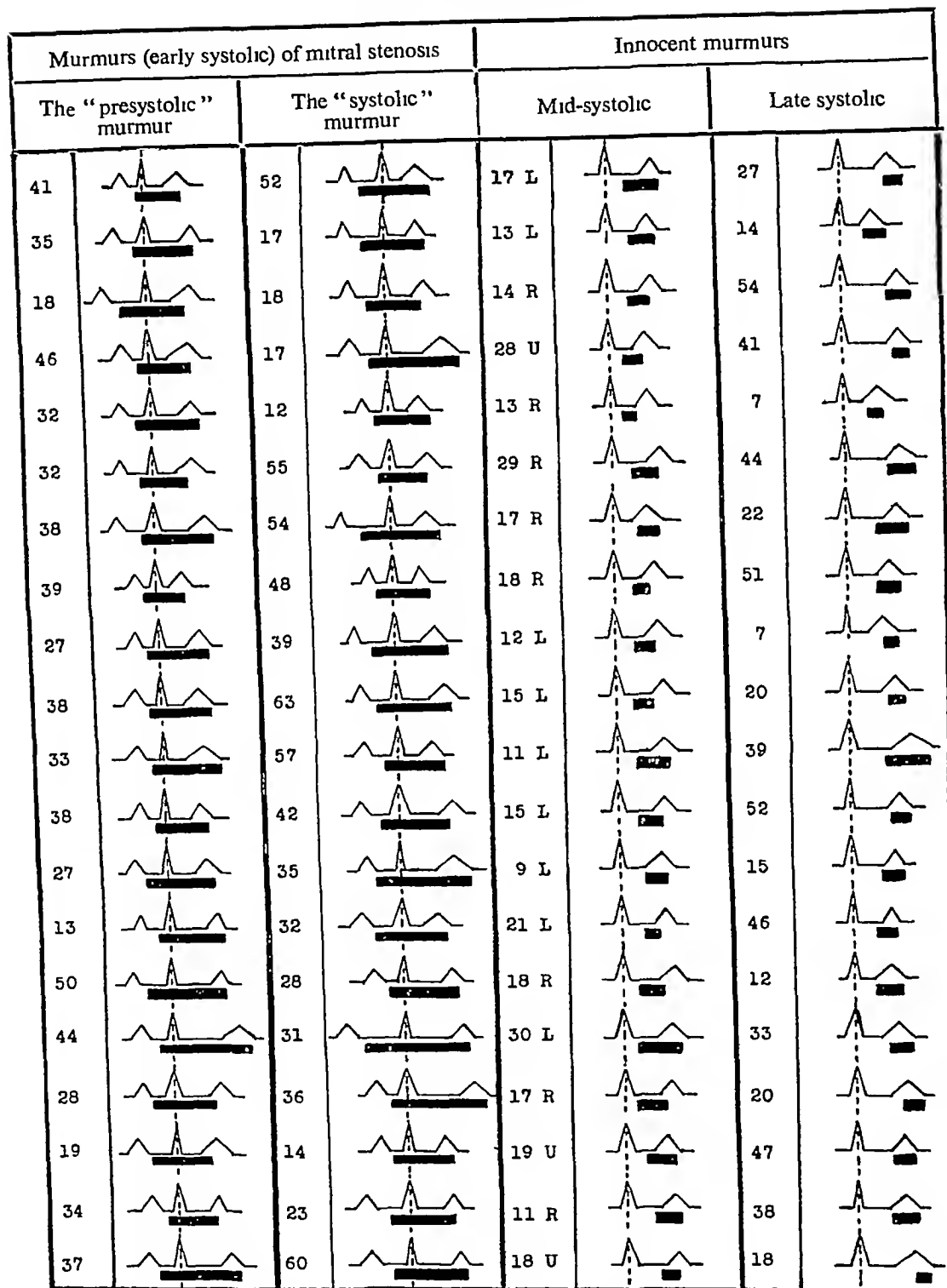
FIG 5 —The position of mitral systolic murmurs (represented by black lines) in relation to the electrocardiogram in 40 patients with mitral stenosis (20 with a presystolic and 20 with a systolic murmur), and in 40 healthy subjects with innocent murmurs (20 with the murmur in mid-systole and 20 in late systole)   Figures denote ages   Letters in the third column designate the clinical classification for innocent murmurs, thus R is the murmur of Reclining Posture, U the murmur of Upright Posture, and L the Loud Variety

could be allocated to four groups   The investigation has emphasized the importance of this clinical classification in the identification of this murmur, and the characteristic signs summarized in Table I, will now be described for each group   It bears repetition that the value of the phonocardiogram has so far been found not in its routine use for the detection of innocent murmurs, but to confirm the validity of the clinical signs assigned to innocent murmurs, and this it has done

TABLE I

DISTINCTIVE CLINICAL FEATURES IN 330 HEALTHY SUBJECTS WITH AN INNOCENT MURMUR

Special features	The murmur in mid-systole (262 cases)				The murmur in late systole (68 cases)
	The murmur of reclining posture (135)	The murmur of upright posture (80)	The loud variety of murmur (7)	The parasternal murmur (40)	
Age	Young subjects	Young adults	Young subjects	Older adults	Any age
Character	Blowing or roughish	Blowing or roughish	Blowing or roughish	Blowing or roughish	Blowing or roughish
Intensity	Not loud	Not loud	Loud	Loud	Loud
Effect of deep inspiration on intensity	Disappears to auscultation	Disappears to auscultation	Persists	Persists	Persists
Effect of posture on intensity	Louder in reclining posture	Louder in upright posture	Trivial	Trivial	Trivial
Effect of posture on distribution	Murmur appears in pulmonary area on reclining	None	Towards axilla in upright, and towards base in reclining posture	None	None

THE MURMUR OF RECLINING POSTURE

Among the clinical signs common to cases in whom a subsequent special examination showed no evidence of heart disease was the fact that the murmur was louder in the reclining than the upright posture   By itself such a sign cannot be distinctive, but along with others it eased the recognition of the murmur and this justified the name given to it   This group of innocent murmur held 135 of the 330 cases   Children under 10 were not accepted, 88 cases were between the ages of 10 and 19, 36 between 20 and 29, and 11 between 30 and 39, there was none older than 40 so that the murmur is confined to younger subjects   The murmur was never loud or long and because of this it was little conducted, and with few exceptions it was dispelled by deep inspiration   It was best heard over an area just internal to the mitral area   Tachycardia was without constant effect on its intensity   The murmur was always louder in the reclining posture, and it was characteristic of this group that as the subject reclined a murmur appeared in the pulmonary area   In 12 instances the pulmonary murmur was also audible in the upright posture, and, if so, the murmur was louder in the reclining posture at the pulmonary area than at the mitral   In 15 cases the pulmonary murmur added in the reclining posture was conducted towards the aortic area, but a silent area separated the pulmonary and mitral murmurs as in the other cases

All 135 cases were referred for special cardiological examination because a diagnosis of valvular disease had been entertained, usually by more than one medical practitioner   In 38 there was a long history of cardiac invalidism on the grounds that the murmur indicated mitral disease   Twenty-five cases had suffered some time from rheumatic fever or chorea, and for that reason the murmur had gained a greater significance, and organic heart

disease was regarded as the cause with greater confidence Among restrictions, handicaps, and penalties, to which subjects in this group had yielded, were rest in bed for several months, prevention from taking part in games and physical exercises including swimming, allocation to a low health category by Military Recruiting Boards denying admission for military service, dismissal from certain civilian occupations, and failure to enter others

THE MURMUR OF UPRIGHT POSTURE

This murmur was found in 80 of the total of 330 cases Thirty-nine were between the ages of 10 and 19, 22 between 20 and 29, 16 between 30 and 39, and 3 between 40 and 43 A comparison of the age incidence of this group with the previous one shows that the murmur of reclining posture belongs to a rather earlier age than the murmur of upright posture, thus, for the former group the murmur was twice as common at ages under 20 years as over, and for the latter group it was twice as common at ages over 20 as under

Unlike the murmur of reclining posture, this murmur was better heard in the upright posture Although diffuse in its distribution over a small area internal to the mitral it was never conducted afar because it was never loud, and except for 13 instances it disappeared on deep inspiration

All 80 subjects had been suspected by one or more medical practitioners of having mitral disease, and in 18 unwarranted invalidism had been enforced As in the previous group so also in this one, such invalidism was commoner in the presence of a past history of rheumatic fever or chorea, and this applied to 13 cases

THE LOUD VARIETY

Although only 7 examples of this murmur are cited it is likely that it is a good deal commoner than this figure suggests because the low incidence here is partly explained by the fact that its innocent nature was only recognized with certainty towards the end of this investi-
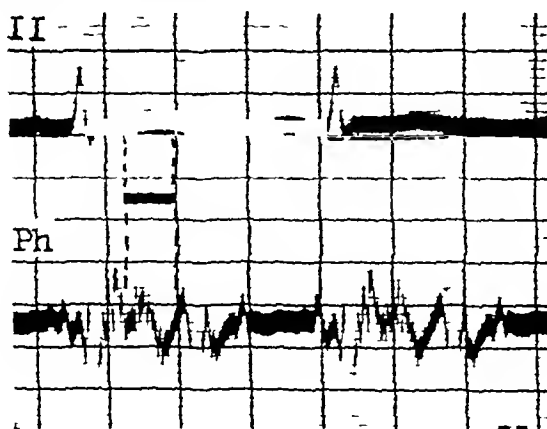
Fig 6 —The loud variety of innocent systolic murmur

gation, more cases have come to my notice since the present analysis was completed Indeed the small number is not a measure of its importance for this lies in the certainty with which the murmur is mistaken for one indicating mitral disease The ages ranged from 11 to 20 years so that this murmur, too, appears to be confined to young subjects

The murmur was loud but never rough or harsh like other varieties one of its peculiar features was its fineness, demonstrated by its roughish, blowing, or whiffy character It was

lessened but never abolished by deep inspiration, and as in the case of other innocent murmurs, which were obscured or diminished by deep inspiration, it was noticed that when respiration was resumed the murmur regained its customary intensity only after two or three heart beats It was diffuse in its distribution and in the cases examined it spread towards the axilla in the upright posture when it was loudest, and towards the sternal border and pulmonary area in the reclining posture

On careful auscultation it was possible, unless hindered by tachycardia, to identify its position in mid-systole and the small gap between the first heart sound and the murmur, but a phonocardiogram was desirable to support the clinical diagnosis in this instance, for because of its intensity the murmur suggested the diagnosis of mitral disease, the phonocardiogram (Fig 5 and 6) gave proof of its innocence by placing the murmur in mid-systole and by showing the absence of murmurs characteristic of mitral stenosis

The Parasternal Murmur

This murmur was present in 40 of the 330 cases   Twelve were between the ages of 10 and 19, 9 between 20 and 29, 13 between 30 and 39, and there were 6 over 40

Because the murmur was loud it was never abolished by deep inspiration   It was audible for a little distance away from its point of maximum intensity in the fourth intercostal space at the left border of the sternum   Posture had no great influence on its intensity   Although loud it was never harsh, and it was usually described as roughish, blowing, or whiffy, terms that emphasize the fineness of the vibration   The murmur was never associated with a thrill, which helped to distinguish it from the murmur of ventricular septal defect heard in the same position   Sometimes it was possible to make out on clinical auscultation that the murmur occupied mid-systole because of the short gap which separates the first heart sound from the murmur that follows it   This was told with certainty by the phonocardiogram (Fig 7 and 9) which demonstrated the murmur starting a little distance beyond the S line and later than the murmur of ventricular septal defect which starts at the S line (Fig 8 and 9)
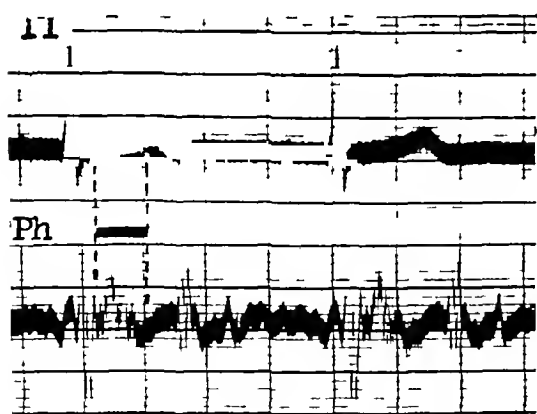
FIG 7 —The innocent parasternal murmur
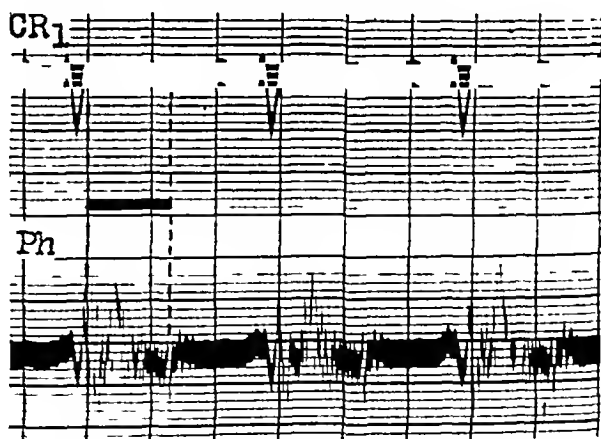
FIG 8 —The murmur of ventricular septal defect

The electrocardiogram was useful in this group of cases because it was always normal, whereas it was often abnormal in the cases of ventricular septal defect studied alongside the innocent group   In the same way cardioscopy was indispensable for there was never enlargement of the heart in the cases showing the innocent parasternal murmur, while in the patients with the congenital lesion there was often some degree of right heart enlargement

Owing to the peculiar site of the murmur most of these cases had been regarded as instances of congenital heart disease, but some had been diagnosed as mitral disease, especially those with a past history of rheumatic fever, 10 in number
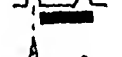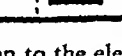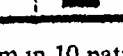
Ventricular septum defect		Innocent parasternal murmur	
29		36	
16		37	
10		19	
11		21	
17		36	
17		41	
11		21	
6		38	
45		12	
21		23	

FIG 9 —Position of murmurs in relation to the electrocardiogram in 10 patients with ventricular septal defect, and in 10 subjects with innocent parasternal murmur   Numerals denote ages

THE MURMUR IN LATE SYSTOLE

In this important group there were 68 cases   Seventeen were between the ages of 10 and 19, 12 between 20 and 29, 15 between 30 and 39, 13 between 40 and 49, and 6 between 50 and 59, there were 5 over 60 years of age
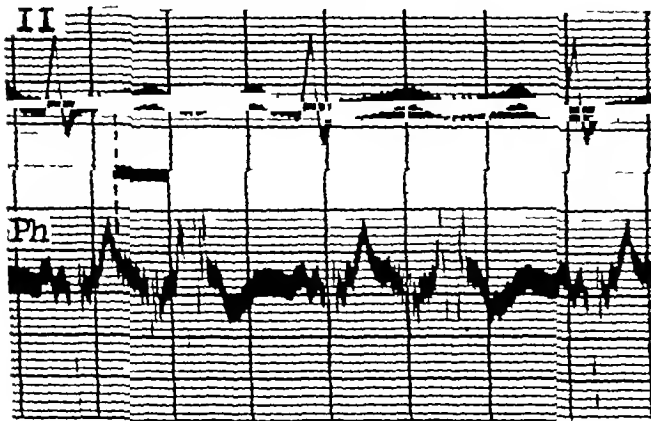
FIG 10 —The innocent murmur in late systole
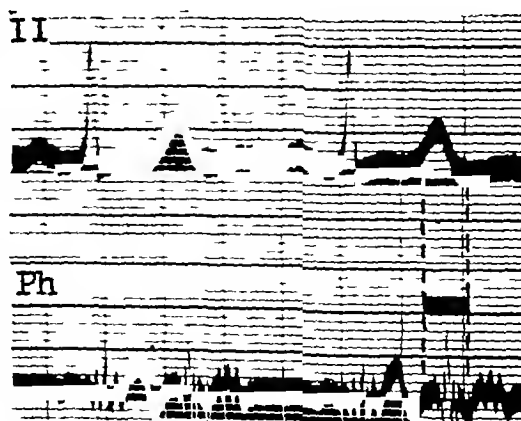
FIG 11 —The innocent murmur in late systole

The murmur was loud and for this reason it was heard some distance away from its site of maximum intensity in the mitral area, and it was still audible on deep inspiration Posture had no specific effect on the murmur although in many it was a little louder in the upright posture   The quality of the murmur was never rough or harsh, and in common with other innocent murmurs it was described as roughish or blowing   Its most distinctive feature was its lateness in systole for it was placed nearer to the second than the first heart sound showing an obvious gap between the first sound and the murmur   The phonocardiogram (Fig 5, 10, and 11) always confirmed its position towards the end of systole, it started near the commencement of the T wave and seldom lasted till the end of systole and the second heart sound   In other cases, not included here, a clear *sound* appeared in late systole initiating an innocent kind of triple heart rhythm

As the murmur was so loud and as it occurred in subjects of all ages, it proved even a greater source of unwarranted invalidism, for once consigned to this inferior health category it lasted for a lifetime because the murmur lasted as long

SUMMARY   INNOCENT MURMURS

The common incidence of innocent murmurs and the unwarranted cardiac invalidism resulting from it give to the problem of distinguishing them from murmurs arising from heart disease a priority unequalled by any other in clinical cardiology   There is urgent need to set a clinical and cardiographic pattern for this murmur, which will make it easy to recognize   The fact that there is as yet no clue to the mechanism of its production need not promote theoretical speculation as to its cause for that might hinder rather than help in its diagnosis   From a study of 330 healthy subjects presenting a murmur, it became possible on clinical grounds alone to recognize its innocent character by placing the cases in five groups (see Table I) which have been named according to the main clinical feature   Thus, the murmur of *reclining posture* was roughish or blowing in character and was confined to young subjects, it was uncommon after 30 and absent after 40 years of age   The murmur was not loud and for that reason it was often removed by deep inspiration   It was loudest in the reclining posture, and with this posture a murmur developed in the pulmonary area   Sometimes this last murmur was audible in the upright posture too, and in this circumstance in the reclining posture it was louder in the pulmonary than mitral area   The murmur of *upright posture* was also confined to younger subjects and the oldest case was 43   It was roughish or blowing in character and was best heard in the upright posture   A *loud* variety of innocent murmur was less common, but its loudness invariably caused it to be mistaken for the systolic murmur of mitral disease   hence its importance   It occurred in young subjects   Change of posture affected the distribution of the murmur more than its intensity, so that in the upright posture it became louder towards the axilla, and in the reclining posture upwards and towards the sternum   The *parasternal* murmur was loud and was best heard in the fourth intercostal space near the left border of the sternum, but it was never accompanied by a thrill as the murmur belonging to ventricular septal defect usually is   The murmur in *late systole* was loud and was roughish in character   It occurred at all ages   It could be told easily by clinical auscultation for the murmur was placed nearer to the second than the first heart sound

The phonocardiogram confirmed the validity of this clinical classification   In the first four varieties the murmur was recorded in mid-systole, and in the last variety in late systole   In none did the tracing show a diastolic murmur

II THE MURMURS OF MITRAL VALVE DISEASE

The diagnosis of long standing mitral stenosis presents no difficulty as a rule for it produces obvious physical signs   When the lesion is early its recognition may prove difficult,

while the addition of hypertension and/or of auricular fibrillation, especially when the heart is rapid, may confound the diagnosis   Great help in giving to certain auscultatory signs their true significance has come from radiology, even the presence of unusual physical signs may not prevent diagnosis of the valvular lesion after taking stock of the size and shape of the heart at cardioscopy   None the less, since the left auricle impresses the œsophagus in health, the slight departure from the normal found in early distension of the left auricle in mitral disease, often leaves a difficulty in the radiological interpretation   Two other circumstances obstruct the radiological diagnosis of mitral stenosis, first, in rare instances of undoubted mitral stenosis the heart at cardioscopy is unaltered in shape and size, secondly, when the left ventricle is enlarged from hypertension or aortic valvular disease, it deepens the left auricle impression in the right oblique view in much the same way as does the distended left auricle of mitral stenosis, although help in the differentiation can come from examination in the left oblique view   These difficulties compel a critical re-examination of the auscultatory signs of mitral disease and an inquiry into the graphic registration of those murmurs made familiar by auscultation   The three murmurs associated with mitral disease will now be considered separately

The Presystolic Murmur

A phonocardiogram was recorded in 33 patients with mitral stenosis who showed the characteristic presystolic murmur on auscultation   The association of a murmur and a loud first sound had produced a rough note which might be represented as *thurr-rupp*, this was
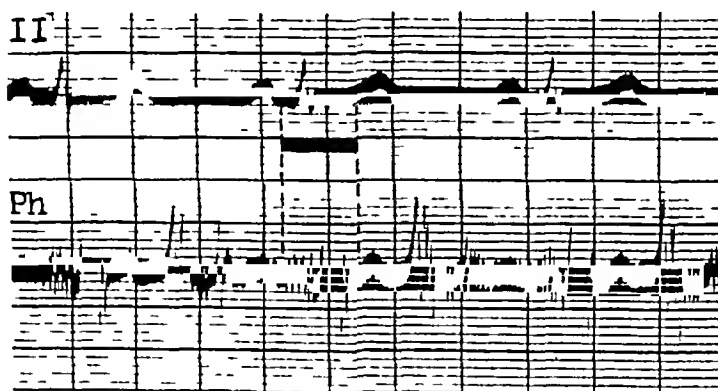
FIG 12 —Auricular murmur in mitral stenosis where auscultation showed a presystolic murmur
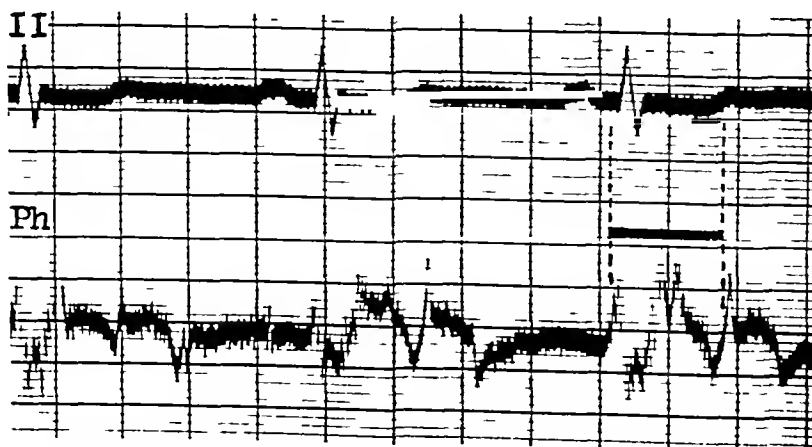
FIG 13 —Auricular murmur in mitral stenosis where auscultation showed a presystolic murmur

louder and more abrupt than splitting of the first heart sound found in healthy subjects, which might be represented as *r-rupp* Although a crescendo character is customarily described for the presystolic murmur, such an effect is an auditory impression gained during auscultation for graphically the murmur does not show such progressive intensification

In 31 cases the murmur started during the P–R period of the electrocardiogram (Fig 5), it started at the end of the P wave in 14 (Fig 12), early in the P–R period in 8, and late in 9 (Fig 13) In the light of this graphic representation the term presystolic may be used as by this is meant pre-ventricular-systole, but since the murmur takes place during systole of the auricle, the term *auricular systolic murmur* is more informative, and is the name that best conforms to its scientific interpretation In only 2 cases did the murmur, which clinically was indistinguishable from the one heard in the other 31 patients, fail to show earlier than the S line, this marking the early phase of ventricular contraction In both it was noticed that the P wave showed a small voltage, its amplitude being less than one millimetre

In 19 cases a mid-diastolic murmur was continued into the period of auricular systole and joined with the auricular murmur, while in the remaining 14 patients the diastolic murmur had almost spent itself before the auricular systolic murmur started

Occasionally the friction sound in acute pericarditis (Fig 14) can simulate the auricular
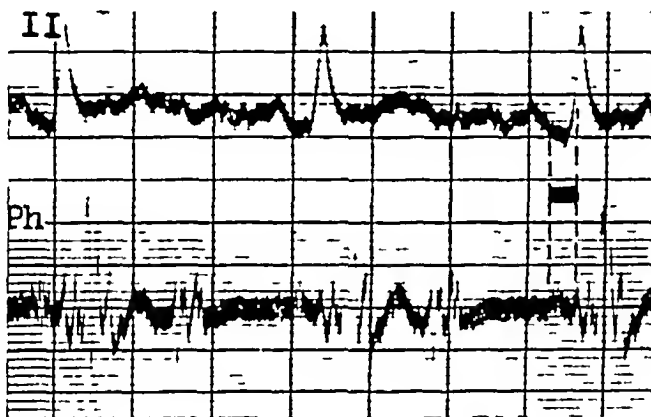
FIG 14 —Friction sound during auricular systole in acute pericarditis

murmur of mitral stenosis, but is easily distinguished on clinical grounds—its disappearance in a few days, the absence of a mid-diastolic murmur, and the history of the illness

THE SYSTOLIC MURMUR

A phonocardiogram was recorded in 41 patients with undoubted mitral stenosis in whom a mitral systolic was heard on auscultation, but a presystolic murmur could not be elicited although it was sought in each case after inducing tachycardia

In 33 the murmur commenced during the P–R period of the electrocardiogram (Fig 5), in 8 it started at the end of the P wave (Fig 15), in 11 early in the P–R period, in 14, late (Fig 16) Such findings are surprising for they are the same as those in the series of patients with mitral stenosis showing a presystolic murmur There were 8 cases in which the murmur commenced at the S line marking the early part of ventricular contraction (Fig 17), in each of these cases a mid-diastolic murmur was present In common with the two similar cases in the presystolic murmur series, they showed a small voltage of the P wave in the electrocardiogram with an amplitude less than one millimetre

In 13 cases a mid-diastolic murmur was continued into the period of auricular systole and joined with the auricular murmur, while in the remaining 28 patients the diastolic murmur had almost spent itself before the start of auricular systole
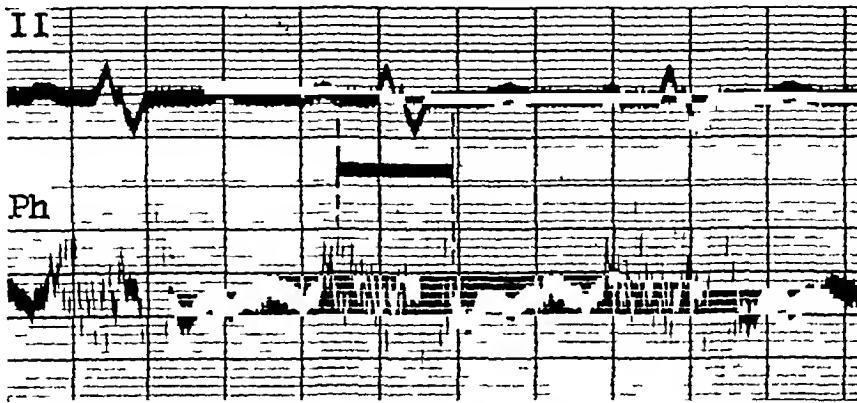
FIG 15 —Auricular murmur in mitral stenosis where auscultation showed a systolic murmur

FIG 16 —Auricular murmur in mitral stenosis where auscultation showed a systolic murmur

FIG 17 —A murmur in mitral stenosis where auscultation showed a systolic murmur, which commences at the S line Confirmation of mitral stenosis is found in the mid-diastolic murmur following the third heart sound

THE MID-DIASTOLIC MURMUR

A further significant finding in this investigation has been the invariable presence in the phonocardiogram of a mid-diastolic murmur it was present in every one of the 74 cases, 33 of which had a presystolic murmur and 41 a systolic murmur on auscultation The murmur was attached to the end of the third heart sound, and in 32 cases it was continued into the period of auricular systole and was joined to the auricular systolic murmur (Fig 18), while in the remaining 42 patients the diastolic murmur had almost disappeared when the auricular murmur started

On clinical auscultation the mid-diastolic murmur was not elicited in 11 patients, and in 12 others the added sound was thought to be the third heart sound devoid of a murmur The murmur was heard in the remaining 51 patients, but in 21 of these it was necessary to

listen towards the axilla with the patient inclined on the left side after induced tachycardia In many cases with a rapid heart rate, however, the mid-diastolic murmur found on auscultation appeared to be contiguous with the auricular systolic murmur following closely on it
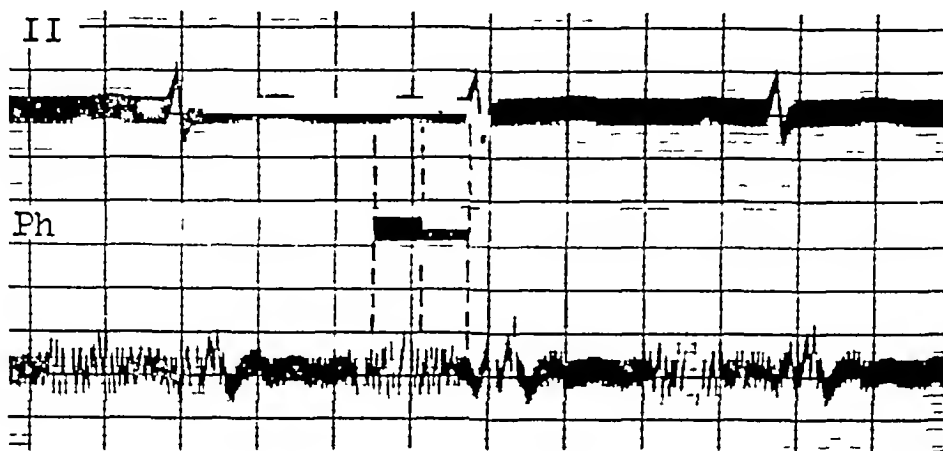
FIG 18 —The mid-diastolic murmur of mitral stenosis, which is contiguous with the auricular murmur

AURICULAR FIBRILLATION IN MITRAL DISEASE

Naturally, in auricular fibrillation the auricular systolic murmur was absent although often the mid-diastolic murmur approaching the ventricular part of the first heart sound provided a clinical impression of a presystolic murmur

A phonocardiogram was taken in 20 patients with mitral stenosis and auricular fibrillation, in each the systolic murmur started at the S line, i e at the onset of ventricular contraction (Fig 19) This was unlike auricular fibrillation in other conditions showing a systolic murmur such as hypertension where the murmur started later and in mid-systole (Fig 20) Phono-
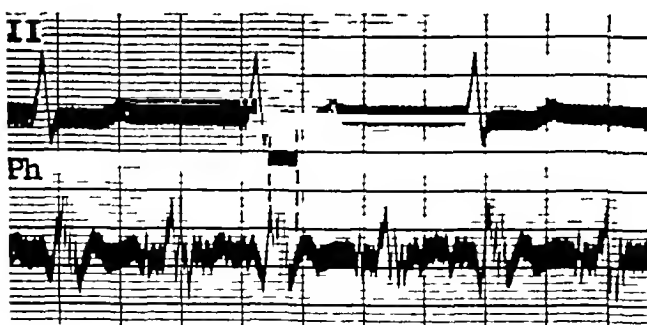
FIG 19 —The systolic murmur in mitral stenosis with auricular fibrillation, which starts at the S line
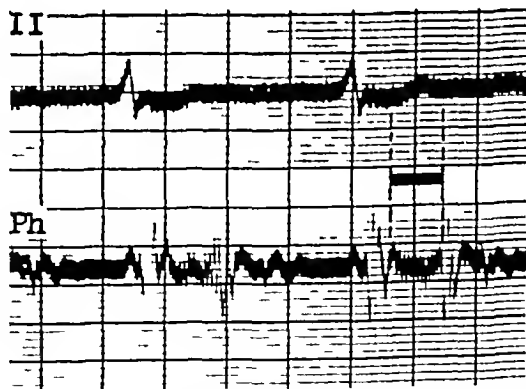
FIG 20 —The systolic murmur in hypertension with auricular fibrillation, which starts in mid-systole and some way after the S line

cardiographically, therefore, the diagnosis of mitral disease as the cause of fibrillation is assisted by a regard of the place of the systolic murmur, confirmation comes from finding a mid-diastolic murmur in every case   During a long diastolic phase this murmur was isolated in mid-diastole, but with a shorter diastolic period the murmur was continued up to the ventricular part of the first heart sound of the next beat

SUMMARY   MURMURS OF MITRAL DISEASE

With two exceptions in 33 patients with mitral stenosis who had a presystolic murmur, the phonocardiogram showed the murmur starting within the P–R period, that is, during auricular systole, in the two exceptions where the murmur started at the S line marking the early phase of ventricular contraction, it was noticed that the P wave of the electrocardiogram was less than one millimetre in amplitude

The most significant finding in this investigation is that in patients with mitral stenosis where a systolic murmur was heard on auscultation and a presystolic murmur was not elicited even after inducing tachycardia, the murmur also started during the P–R period in the majority (33 out of 41)   Thus, the systolic murmur of mitral disease, like the presystolic murmur, was produced by auricular systole in such cases   The conditions in the 8 exceptions tallied with those found in the two similar examples in the presystolic murmur series, in that the murmur started at the S line, and was associated with a small P wave (of less than one millimetre in amplitude)

These graphic findings endorse the specific role of auricular contraction in producing the systolic as well as the presystolic murmur and support the view that a diagnosis of mitral stenosis should be applied to mitral valve disease whichever of the two murmurs it presents on clinical auscultation   Even in the 10 cases (2 with presystolic and 8 with systolic murmur on auscultation) where the murmur in the phonocardiogram was seen no earlier than the S line the application of the term " mitral incompetence or regurgitation " would be inaccurate because in each of them there was a mid-diastolic murmur to give proof of mitral stenosis Indeed a mid-diastolic murmur was present in the phonocardiogram in each of the 74 cases of mitral disease, whether with a presystolic or systolic murmur, emphasizing on the one hand its value in a case with equivocal clinical and radiological signs, and on the other hand the need of searching diligently for this murmur under the most favourable circumstances, namely to listen attentively after inducing tachycardia and inclining the recumbent patient to the left side   A detailed analysis of the phonocardiograms from the two series of patients failed to explain what determined in mitral stenosis whether the murmur should be of the presystolic or systolic kind   It neither depended on the length of the P–R period nor on the duration of the diastolic phase, nor was the graphic registration of the murmur distinctive for each group   It can only be surmised that the intensity and abruptness of the first heart sound decides the presence or absence of the rough quality that typifies the presystolic murmur

PHONOCARDIOGRAMS OF AURICULAR MURMURS
FROM A CASE WITH MITRAL STENOSIS AND HEART BLOCK

BY

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It is well known that an auricular sound can sometimes be recognized by means of the stethoscope or phonocardiogram In some instances it can be shown that the so-called first heart sound consists of a fusion of an auricular sound with a ventricular sound, and this may be evident in cases with prolongation of the P–R interval This, however, is generally not easily recognized, otherwise there should be a presystolic sound or a double first heart sound in all cases of partial A–V block

In their monograph, Orias and Braun-Menendez (1939) state that three different acoustic phenomena contribute to the auricular first heart sound, namely—and in the following order—vibrations in the contracting auricles, the dilatation of the ventricles during their filling with blood, and vibrations in the mitral and tricuspid valves at the closure of the corresponding orifices at the end of the auricular systole The first mentioned can only be studied from the œsophagus, the other two from the præcordium also

It is stressed by different authors (Orias and Braun-Menendez, 1939, Bramwell, 1935, and Cossio and Fongi, 1936) that the auricular first heart sound will be increased during conditions, when the blood stream through the auriculo-ventricular orifices is increased or hastened (thyrotoxicosis, hypertension, and mitral stenosis with left auricular hypertrophy) It is also easy to understand that the rigidity of the valves in mitral stenosis might change the auricular sound to a murmur If the statement of Levine (1941) is true, that seven-eighths of the blood stream from auricles to ventricles passes the orifice only on account of pressure-equalization, whereas the last eighth is caused by auricular contraction, it will be clear that only the presystolic murmur in mitral stenosis is caused by auricular systole This is also evident from the fact that the presystolic part of the diastolic murmur disappears when auricular fibrillation starts and there is no regular auricular systole

We have recently studied a case of mitral stenosis with complete heart block, where the auricular murmur is very beautifully demonstrated on the phonocardiogram As such cases are rare, according to Lewis (1944), and also from our own experiences, it might be of interest to report one instance The physical and phonocardiographic quality of the sound places it in the class of *murmurs*

CASE REPORT

A woman, 49 years old, whose mother and grandfather and uncle had organic heart disease, had diphtheria in childhood and acute rheumatic fever at the age of 18 At the age of 25 dyspnœa and irregular heart action developed and the diagnosis of organic heart disease was made She had a second attack of rheumatic fever four years later, after which there was increasing breathlessness, nocturia, pain in the chest, and irregular heart action

The examination at the Sabbatsberg's hospital in 1943 revealed slight pre-tibial œdema and

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dyspnœa on action   Over the whole heart systolic and diastolic murmurs with their maxima over the heart base were heard   The rhythm seemed to be regular with some few premature beats   The blood pressure was 175/110   X-ray of the heart was normal, the size being 415 c c per square metre body surface   The cardiogram revealed a partial A-V block, which could not be influenced by atropine, alternating with complete heart block   The degree of the block seemed to be related to the course of the subjective symptoms

At a fresh examination in 1945 there was, besides the above-mentioned murmurs, a peculiar, changing, possibly presystolic murmur over the apex, which made the occurrence of an auricular murmur suggestive   There was now complete heart block and right axis deviation in the cardiogram, as compared with normal axis in 1943

Phonocardiograms (Fig 1) confirmed this origin of the new murmur   In all frequencies—especially the lower ones—there was besides the harsh systolic murmur over the apex, a murmur that was constantly related to the auricular activity (P wave)   When the auricular systole appeared on its " normal " place in the chain of events, the auricular murmurs caused a typical presystolic murmur   Otherwise it was atypically located in the heart cycle   When
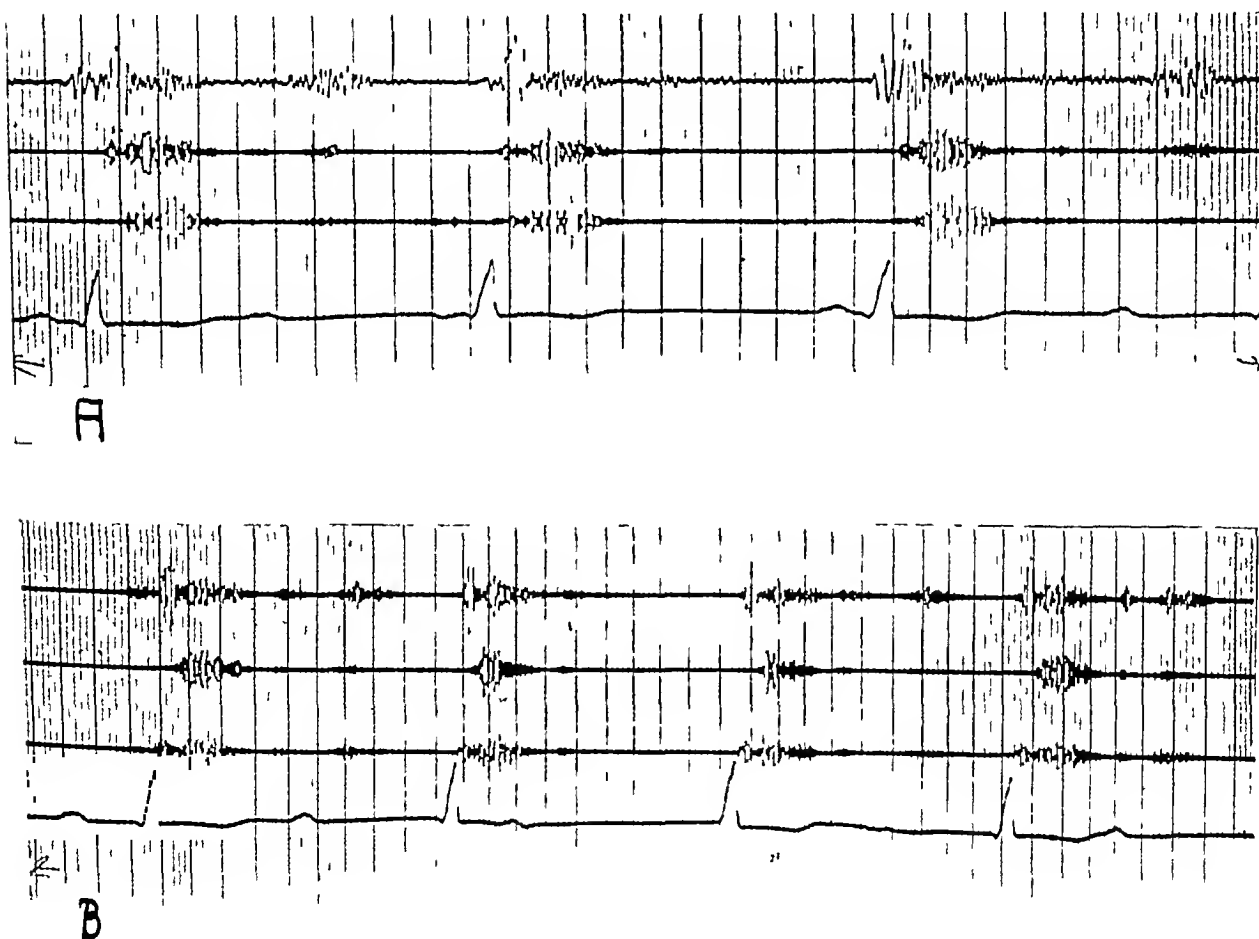
FIG 1 —Calibrated phonocardiograms of the case described   (A) The upper three lines show the phono-cardiograms with frequencies 15–100, 170–290, and 400–850 cycles, and the lowest line the electrocardio-gram   (B) The upper three lines show the phonocardiograms with frequencies 80–180, 260–520, and 15–850 cycles, and the lowest line the electrocardiogram   In each instance the auricular contraction (P wave) is accompanied by the specific auricular murmur, independent of any relationship to the ventri-cular activity

C

it occurred independently it was evident that the murmur was not of the crescendo type, as has often been alleged   This is, as White (1944) has pointed out, an illusion caused by the close relationship between the presystolic murmur and the first heart sound, in which it is finally absorbed   In the case presented the auricular murmur was recorded on the phonocardiogram 0 16 sec after the beginning of the P wave, which approximately corresponds to the findings of Orias and Braun-Menendez (1939)   The duration was 0 14–0 16 seconds

SUMMARY

A case of rheumatic heart disease with aortic stenosis and regurgitation and mitral stenosis is reported, where the existence of a complete heart block clearly demonstrates the auricular origin of the presystolic murmur in mitral stenosis

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CHRONIC AURICULAR TACHYCARDIA

There are exceptions to all the criteria employed for the differentiation of paroxysmal auricular tachycardia from other forms of rapid heart action   Nevertheless, the three most constant features are the sudden onset, the short duration (rarely more than ten days), and the sudden termination   We have had the opportunity of observing a case, which while falling into the category of paroxysmal tachycardia, yet differed from the classic type in its chronicity and in its response to treatment

Case History   A man, aged 31, was admitted to Southmead Hospital on May 27, 1946, with persistent tachycardia   There was no past history of scarlet fever, rheumatism, or diphtheria   A paternal uncle gave a history of bouts of tachycardia since adolescence, lasting anything from minutes to two days

He was taken prisoner by the Japanese in Bandoeng, Java, on March 8, 1942   As a prisoner he was made to work hard and given poor rations   During 1942 his diet consisted of 400–500 g of rice daily, a variable quantity of local green vegetables, and an occasional small ration of meat   Later the rice was cut down to about 100 g a day and was supplemented by an addition of tapioca bread, meat practically disappeared from the diet   During his captivity he had three attacks of bacillary dysentery and dengue once   In 1942, cases of nutritional neuropathy began to occur and were seen in ever-increasing numbers   He escaped with only slight numbness down both shins, starting two months before release   In September 1945 he was repatriated and had an adequate diet

During the early part of 1944 he began to get attacks in which he was conscious of his heart beating rapidly and apparently regularly   These attacks lasted about half an hour, and occurred very irregularly   The initial ones stopped spontaneously, and later he learnt to control them by taking a deep breath, leaning forward, and sometimes breaking wind   His medical attendant stopped one attack by carotid pressure

After he had been subject to these attacks for about six months he found that they persisted longer and were more difficult to terminate   On the ship that brought him back from Singapore in October 1945, some lasted thirty-six hours

On December 11, 1945, he started an attack of tachycardia, and this was noted by a member of a medical board which discharged him from the Services   He stated that this condition had persisted without interruption ever since   In February 1946 he complained of troublesome dyspnœa on exertion, and this increased rapidly thereafter   His ankles did not swell, and he had no præcordial pain   During the first week in May his doctor sent him for an X-ray, and cardiac enlargement was found, together with pulmonary congestion   He was ordered to bed and given 15 mg of vitamin B_1 daily for two weeks with no apparent effect, and subsequently admitted to hospital

Examination   He was found to be well covered, and was not nervous or distressed   There was no cyanosis of the cheeks or mucous membranes   Dyspnœa occurred on slight exertion but not on lying down   No focal infection was found in the teeth or throat   There

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was no thyroid enlargement, no tremor of the outstretched hands, nor was his skin unduly moist   No abnormality was found on examination of the central nervous system

The cervical veins were distended, and the liver was enlarged two fingers' breadth below the costal margin   No signs of pulmonary congestion or effusion into serious cavities were found, and there was no œdema   The apex beat was in the sixth intercostal space in the anterior axillary line   No thrills were felt   The heart was beating regularly at the rate of 168 a minute (Fig 1), the sounds were normal and there were no murmurs   The blood pressure was 105 systolic and 70 diastolic, and showed no postural alteration   Carotid
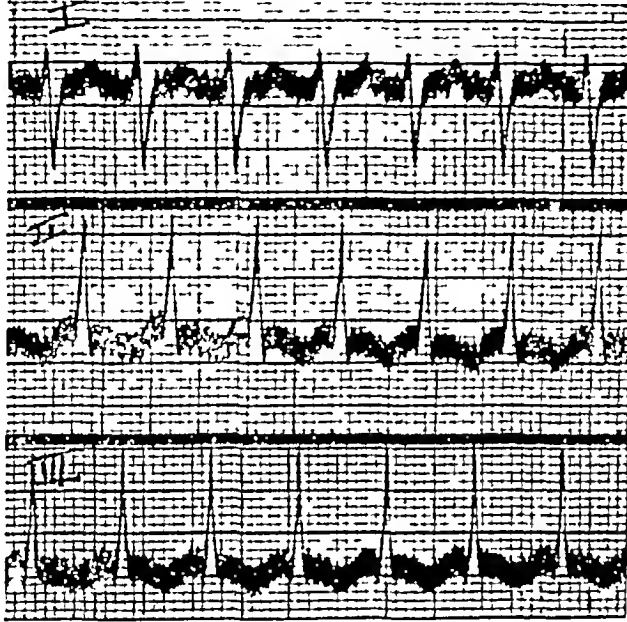
FIG 1 —Initial cardiogram, May 28, 1946   The three standard leads are shown   The rate is 168 a minute and is regular   T is upright in lead I and inverted in leads II and III

and eyeball pressure had no effect on the tachycardia, nor was there any alteration with changes of posture, exercise or phases of respiration

A teleradiogram showed generalized cardiac enlargement and pulmonary congestion The hæmoglobin was 108 per cent, the red blood count 5,300,000, and the white blood count 10,200   The Wassermann reaction was negative   No abnormality was found on examination of the urine   The cardiographic findings, on which a diagnosis of paroxysmal tachycardia was made, will be analysed in a later section

Progress   Quinidine therapy was attempted and abandoned because he was hypersensitive to small doses

On June 12 he was given 9 grains of digitalis, and this dosage was continued daily for eleven days, after which it was reduced to 6 grains   On these large doses of digitalis the pulse rate fell during sleep and also showed a gradual decline during the waking hours   On the 27th he complained of nausea and vomiting, and his pulse fell to 80   Digitalis was discontinued. At this time vagal effects were easily induced   Lying on his left side caused bradycardia, and occasionally even cardiac standstill, both Valsalva's experiment and carotid sinus pressure had the same effect

On July 4 a cardiogram showed that the rhythm had returned to normal, and his pulse rate was 75 a minute   The cervical veins were no longer distended, and the liver was not

palpable   A teleradiogram showed that the transverse diameter of the heart was 4 cm less than on admission

There was a gradual acceleration of the pulse over the next four days to 150 a minute, with a return of the abnormal rhythm in the cardiogram   Because of the fall of the pulse rate during sleep while on digitalis, it was decided to try and assess the effect of the higher centres in the production of the tachycardia   He was anæsthetized with a small intravenous dose of pentothal, but there was no fall in the pulse rate

On July 12 he was given 0 5 mg of prostigmine intramuscularly   Fifteen minutes later carotid sinus pressure restored normal rhythm, which persisted only for five minutes   The following day 1 mg of prostigmine was injected and with the help of carotid pressure a short period of cardiac standstill occurred   The ectopic rhythm returned almost at once   Within half an hour toxic effects, in the form of sweating and muscular twitchings, were noted   On the 14th, 1 5 mg tablets of prostigmine were given three times daily, and on this dosage his pulse tended to remain about 130 a minute   In order to augment the effect of the prostigmine 5 g each of potassium chloride and potassium citrate were given with every dose   This caused severe epigastric pain, sweating, and inability to speak   The dose of potassium salts was reduced by half and this was well tolerated, but appeared to be without effect on the pulse rate, and was, therefore, discontinued

On July 28 he was started on 1 grain of digitalis, four-hourly, in addition to the prostigmine   By August 7 he complained of diarrhœa, so the dose of digitalis was reduced to three times a day   There followed a period during which the heart rhythm and rate were unstable   Short periods of cardiac standstill were followed by a series of normal beats or by an almost immediate return to the ectopic rhythm   Furthermore, it was found that when he was supine his pulse dropped to 83, the rhythm was of sinus origin   On sitting up or standing the ectopic rhythm generally returned and the pulse rose to 120   These postural effects were gradually lost over the next ten days as the pulse rate slowed to 80 and the rhythm reverted to normal   All treatment was discontinued on August 16   The arrhythmia recurred, and by August 24 the pulse had risen to 160 a minute

CARDIOGRAPHIC ANALYSIS

Numerous cardiograms were taken during the period of observation   In the initial curve on May 28, 1946 (Fig 1) the rate was 168, and there was right axis deviation   It was interpreted as showing paroxysmal tachycardia, although at this stage the possibility of flutter had not been excluded

On June 21, ten days after starting digitalis, the cardiogram had appreciably altered (Fig 2)   The rate was 145   An inverted P could be seen in all three leads with a P–R interval of 0 16 sec   T wave was upright in lead I and inverted in leads II and III   Inversion of T in leads II and III is well recognized in paroxysmal tachycardia of long duration (Campbell, 1942)

FIG 2 —Lead II, June 21   The P–R interval is 0 16 sec   The P wave is large and inverted   T is also inverted   This and subsequent cardiograms have been reduced to nine-tenths

Page 21, line 13

★ *For* " 1 5 mg tablets of prostigmine were given "
substitute " 15 mg tablets of prostigmine were given orally".

On June 24 it was found that getting the patient to lie on his left side caused the pulse to become irregular, and even induced sinus block   This is shown in lead II of Fig 3, in which there is a ventricular extrasystole followed by a normal complex with upright P, and then an ectopic P wave (P1), which failed to excite a ventricular contraction because the conducting tissue was in a refractory state   After 1 2 sec a normal beat followed, and then 0 8 sec later there was another normal beat, the T wave of which was succeeded 0 08 sec later by a series of ectopic beats   In the first of these the P–R interval was 0 28 sec, and in the next
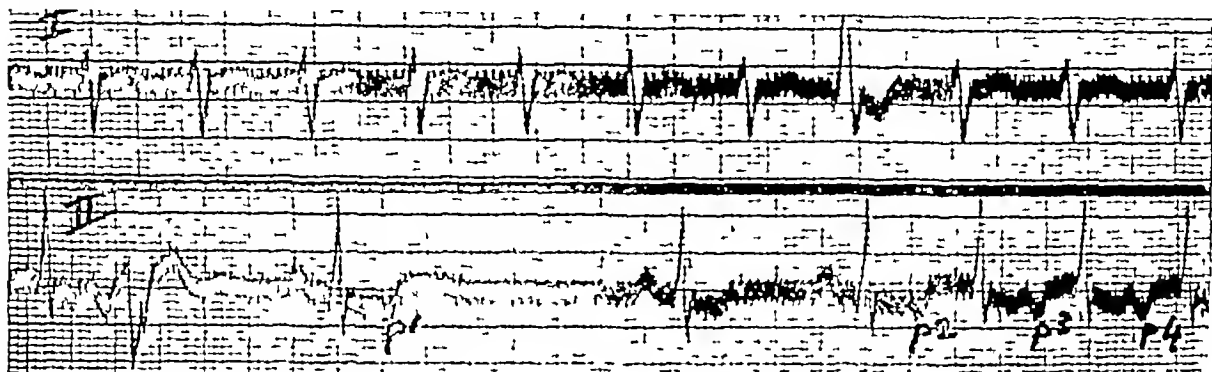
FIG 3 —Leads I and II, June 24   Lead II shows the effect of lying on the left side while on large doses of digitalis

0 2 sec   It was considered that the prolongation of the P–R interval to 0 28 sec resulted from the premature ectopic impulse reaching the A-V junctional tissue so early that it found it in a relative refractory phase   The distance between P3 and P4 in Fig 3 is 0 48 sec, and the distance between P1 and P2 is 2 4 sec, which is five times 0 48 sec   This suggests a parasystolic ectopic rhythm of rate 125 a minute   In lead I there was a ventricular extrasystole that did not alter the fundamental rhythm   With continuance of digitalis the P–R interval increased steadily and by June 26 it was 0 24 sec

On June 28 (when digitalis had been discontinued because of the toxic effects it had produced) a curve was obtained (Fig 4) which demonstrated increased sensitivity to vagal influence   Lead II showed the end of a long period of sinus block produced by Valsalva's experiment, followed by normal beats with inverted T waves   The shape of the T wave in this, as in other curves, was doubtless influenced by the digitalis which had been administered
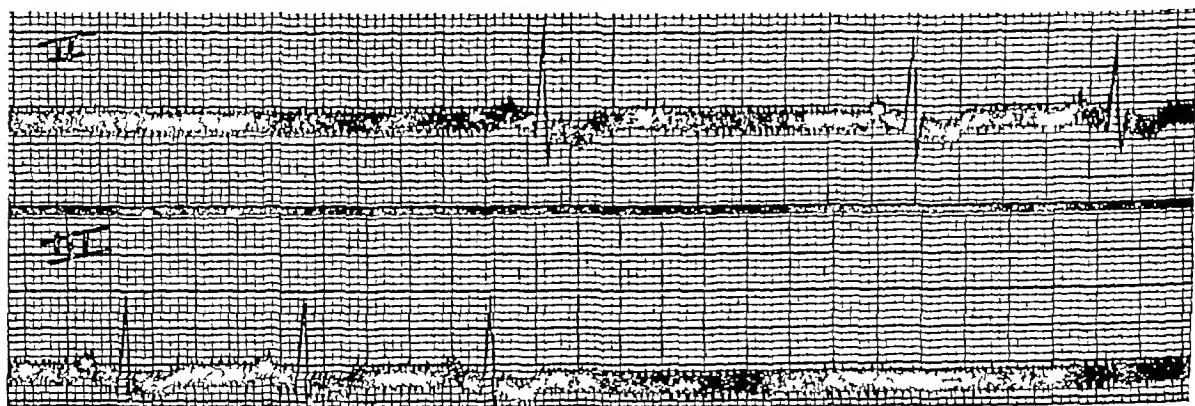
FIG 4 —Leads II and III, June 28   Lead II shows the effect of Valsalva's experiment   Lead III shows the effect of bilateral carotid sinus pressure

Lead III showed the start of another long period of sinus block due to carotid sinus pressure

The effects of 0 5 mg of prostigmine given on July 18 are seen in Fig 5   All these curves were taken on lead II   The first one was obtained before the injection, the second after ten minutes, and the third after a further five minutes during bilateral carotid sinus pressure
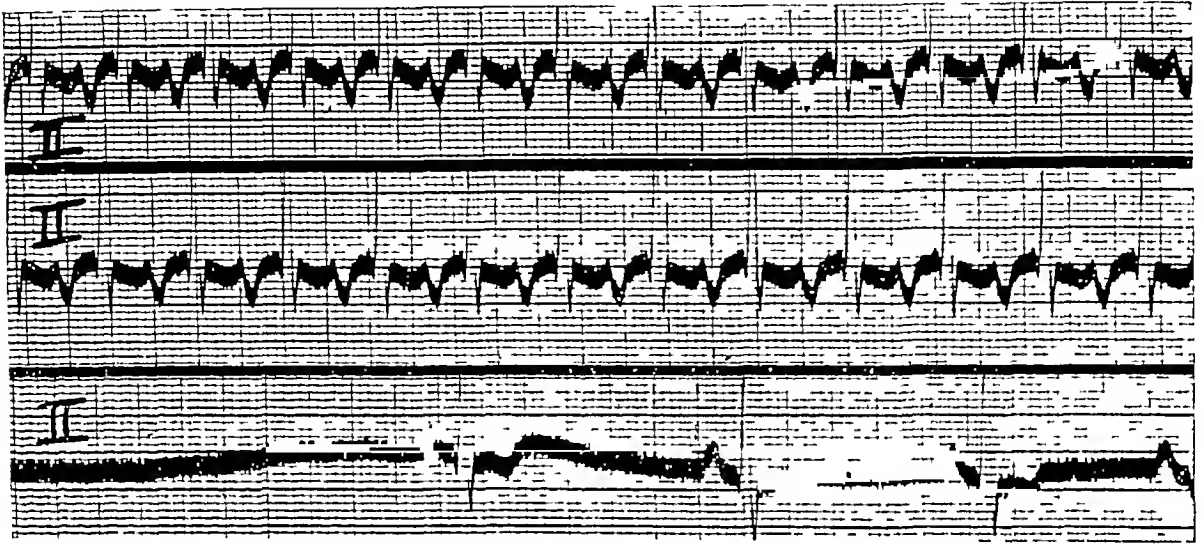
FIG 5 —July 18   All curves are lead II   The top curve was taken before prostigmine 0 5 mg intramuscularly, the middle, ten minutes after, and the lower with bilateral carotid sinus pressure

Fig 6 was obtained on July 4, and shows cessation of the paroxysmal tachycardia   The rate was 75 a minute, and the P-R interval was 0 16 sec   P was upright in all three leads, and T was inverted in leads II and III

The præcordial lead CRI was used to study auricular activity   In Fig 7 the first complex is normal and is followed by an ectopic P which is blocked   There follows, after a pause,
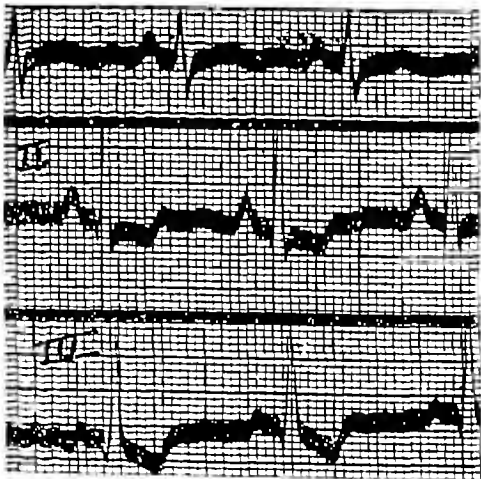
FIG 6 —Leads I II, and III, July 4, showing normal rhythm at the rate of 75 beats a minute   The P waves are upright, and T is inverted in leads II and III

FIG 7 —Præcordial [lead CR$_1$ A blocked ectopic P is clearly shown in the first curve   The change-over from normal to ectopic rhythm can be seen in the lower curve

one further normal complex   In the second curve a series of ectopic beats are shown after a normal complex   In neither of these two cardiograms, nor in others, is there evidence of an A-V block

On August 15 (eighteen days after starting combined prostigmine and digitalis therapy) three cardiograms, each on lead II were taken shortly after 15 mg of prostigmine had been taken by mouth (Fig 8)   In (A) the patient was lying down, a blocked ectopic P (P1) followed the first normal complex, and there followed a long compensatory pause, after which the ventricles responded to an impulse originating in the sino-auricular node   Then followed
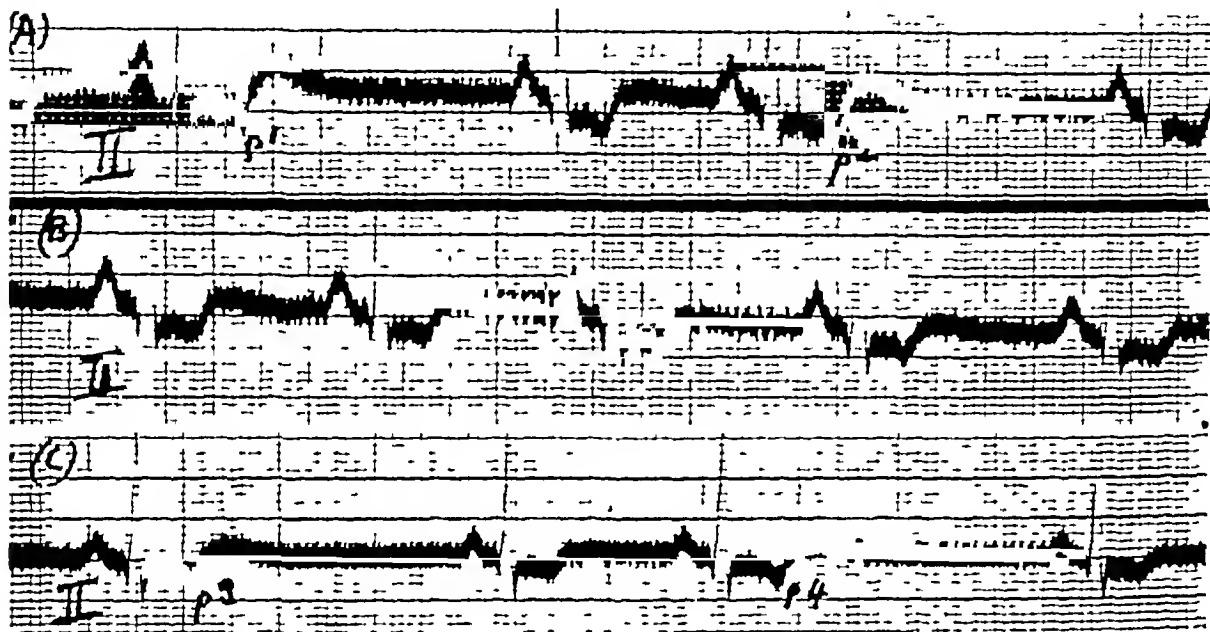
Fig 8 —August 15   All curves are lead II   (A) was taken lying down, (B) sitting up, and (C) sitting up during bilateral carotid sinus pressure   The curves were taken ten minutes after a 15 mg tablet of prostig-mine had been taken by mouth
    (A) and (C) show an ectopic P wave following every second normal complex

yet another normal beat, and then a second ectopic P (P2) bearing the same relation as P1 to its preceding QRS   The effect of this grouping was to produce pulsus bigeminus   In (B) the patient was sitting up   the rate was 60 and regular, and the P–R interval was 0 16 sec , P was upright and T inverted   (C) was taken whilst the patient was sitting up, during carotid sinus pressure, and was very similar to (A)   This showed that recumbency had an effect on the heart in this case equivalent to direct carotid pressure   The intervals P1, P2, and P3, P4 in Fig 8 are the same as P1, P2 in Fig 3 obtained fifty-two days earlier   This finding favours the interpretation of the tachycardia in terms of parasystolic ectopic rhythm

In the cardiogram ectopic P waves, when following normal complexes, show a fixed relation to them, merging with the preceding T, and occur at a time when the junctional tissue is in a relative refractory state   Whether the impulse reaches the ventricle will depend upon the degree of vagal tone   If this is high it will further depress the conductivity and block the impulse

DISCUSSION

Sinus tachycardia can be excluded on the cardiographic evidence of ectopic P waves The progressive lengthening of the P–R interval produced by large doses of digitalis and also the effects of vagal stimulation during therapy with digitalis or prostigmine do not suggest auricular flutter Evans (1944) has stressed the importance of the chest lead CR_1 for the study of auricular activity He is of the opinion that by this means a 2 1 A-V block can always be uncovered in paroxysmal tachycardia and that the difference between this condition and flutter is merely the rate of auricular contractions Campbell (1945) was unable to confirm Evans's findings, as he could exclude an A-V block in at least thirteen of his own sixty-six cases He considers that the shape of the auricular curves and the presence of an iso-electric level rule out flutter, even if a block can be demonstrated We could not find an A-V block in any of our tracings in spite of the use of præcordial leads

The chronicity of the tachycardia and the effects of treatment make this case exceptional Digitalis produced first a tendency for the pulse to drop during sleep, and then a gradual slowing of the cardiac rate At one stage, a combination of digitalis and prostigmine made the pulse rate susceptible to change of posture Each time therapy has been discontinued the arrhythmia has recurred Classification of this case is especially difficult, because a combination of all these features has seldom been recorded

Wilson and Hermann's (1923) patient, in whom tachycardia had persisted for fifteen months at the time he was first seen, appeared to be strikingly similar to ours, but refused further treatment before a final result could be obtained, there were similar periods of bradycardia and standstill after digitalization Maddox (1937) recorded an example of paroxysmal tachycardia lasting at least sixty-nine days in which the attack terminated gradually without the help of digitalis In his case the pulse slowed spontaneously during sleep Rest in recumbency for half an hour or more had a similar effect, inducing a 3 1 block with a pulse rate of 56, and a conduction time of 0 2 sec With exercise the pulse rose suddenly to 168 while the conduction time remained 0 2 sec He did not specifically investigate the effects of posture on the cardiogram Attempts to restore normal rhythm with quinidine, digitalis, acetylcholine, adrenaline, and atropine, were unsuccessful Because of the change of pulse rate with exercise and rest he considered that the extracardiac nerves were mainly responsible This is of interest in view of the exposure of our patient whilst a prisoner to conditions favouring the production of nutritional neuropathy

Miller and Perelman (1945) reported two cases of chronic auricular tachycardia, both with aberrant P waves, which showed striking changes of rate with posture, the rate being slower lying than standing In their first case posture not only changed the rate but also the direction of the P wave in lead I Digitalis abolished the orthostatic acceleration of the pulse rate In their second case, digitalis did not control the tachycardia and there was no response to quinidine or to potassium salts This experience led them to recommend that cardiograms should be taken in three positions, standing, sitting, and lying The importance of this is further emphasized by the reports by Manning and Stewart (1945), and by Holmes and Weill (1945) of the finding of a prolonged P–R interval in healthy young adults, with a decrease to normal on standing Our case resembles those of Miller and Perelman in its chronicity, the arrhythmia has been present for seven months, and can only be satisfactorily controlled by full doses of digitalis and prostigmine However, orthostatic phenomena were not present on admission, and were only obtained for short periods just before full therapeutic effect was reached

The continuous activity of a parasystolic auricular focus with a low degree of exit block under partial control of the extrinsic cardiac nerves, was postulated, though without proof, by Miller and Perelman to explain their findings Only when it can be shown that the

intervals between premature systoles from a common focus are equal, or are multiples of a common denominator, and occur without fixed relationship to the beats of sinus origin, can parasystole be diagnosed with confidence   In our case we have been able to show that periods between ectopic beats from a single focus have a common denominator, but the fixed relation of the ectopic beats to beats of sinus origin which can be seen in the cardiograms is a serious obstacle to the acceptance of parasystole   The fixed relationship to the preceding beat may be explained by the theory of re-entry, but Scherf (1929) has produced evidence to show that these extrasystoles are released from an ectopic centre by the preceding normal beat

SUMMARY

An unusual case of paroxysmal auricular tachycardia has been described   The abnormal rhythm has persisted for seven months without intermissions, except those produced by treatment   Whatever may be the true explanation of the bizarre features presented by this case it is evident that an ectopic focus has come to dominate the heart, and only when the rate has been slowed, with difficulty, by the action of drugs can the sino-auricular node resume command

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CONGENITAL HEART DISEASE WITH ISOLATED INVERSION OF THE ABDOMINAL VISCERA

BY

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The two cases reported illustrate an uncommon type of partial inversion of the viscera, in which the abdominal organs alone are transposed while the heart remains in its normal position. Both were suffering from congenital heart disease, and a subsequent search brought to light several further reports of cardiac malformation associated with a similar transposition of the viscera. This combination cannot, therefore, be regarded as fortuitous, and, in fact, a similar and well-recognized relationship exists between congenital heart disease and another variety of incomplete heterotaxy, in which the heart alone is transposed. Isolated dextrocardia is the subject of two recent reviews, based on large series of cases collected from the literature (Roesler, 1930, and Lichtman, 1931), case reports of heart disease in the presence of isolated inversion of the abdominal viscera are, on the other hand, scanty and so far have not been critically reviewed

CASE REPORTS

Case 1 An Army officer, aged 25 years, was admitted to Guy's Hospital in April 1946 for investigation. Suspicion about his heart arose two years earlier, when a routine radiogram of his chest showed a large heart. His capacity for exercise was normal, in fact, during the previous five years he had undergone several periods of very strenuous training without undue distress. There was no history of cyanosis and he had never suffered from rheumatic fever

He was a well-developed fit-looking man, and was able to take vigorous exercise without dyspnœa. There was no cyanosis or clubbing of the fingers. He was apyrexial and his resting heart rate varied between 50–60, with striking sinus arrhythmia. Owing to this the blood pressure readings were somewhat variable and averaged 145/50. A very forcible apex beat was found 2·5 cm outside the mid-clavicular line. A moderately loud, rough systolic murmur was audible in the second left intercostal space close to the sternum, conducted along that space, as well as to the back, just medially to the left scapula. The pulmonary second sound was accentuated and high pitched. The heart sounds were otherwise normal

All other clinical findings were normal, except that the liver dullness was found in the left hypochondrium, while the right hypochondrium was resonant. Blood pressure readings in the lower limbs were equal to those in the arms and no anastomotic arteries were palpable over the chest wall

X-ray findings In the postero-anterior view (Fig 1A) the heart was enlarged both to the left and to the right, with a maximum transverse diameter of 16 cm in a chest of 29 cm. The convexity of the apical region suggested enlargement of the left ventricle, but the pulmonary conus was also abnormally prominent and the branches of the pulmonary artery, especially the right descending, were strikingly distended. The ascending aorta was displaced to the right, its right border lay 3·5 cm from the mid-line. The gas bubble in the stomach was visible under the right diaphragm. On screening the lower third of the left border of the heart showed marked pulsation, systolic excursion in the region of the conus was also excessive, but no abnormal pulsation was visible in the hilar vessels

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Fig 1—(A) Case 1 Postero-anterior teleradiogram Heart enlarged with increased convexity of the apical region Enlargement of the conus and of the hilar vessels Ascending aorta displaced to the right The stomach lies under the right diaphragm
(B) Case 1 Right (I) oblique view Enlargement of the conus and of the hilar vessels
(C) Case 1 Left (II) oblique view Enlargement of the left ventricle Right ventricle of normal size Displacement of the aorta to the right

The right (I) oblique view (Fig 1B) confirmed the abnormal prominence of the pulmonary conus
The most striking feature of the left (II) oblique view (Fig 1C) was bulging of the left border of the
ventricular shadow, while the right border was, by contrast within normal limits

The electrocardiogram (Fig 2) showed sinus arrythmia, *left axis deviation, and inversion of P II,
P III, and T III*

Diagnosis   In view of the apparent enlargement of the left ventricle and the left axis deviation,
the possibility of aortic regurgitation, sub-aortic stenosis, coarctation of the aorta, or of hypertension
was considered, but no further evidence was found in favour of any of these conditions

The prominence of the pulmonary conus, the widening of the main branches of the pulmonary
artery, the forcible pulsation of the apex and of the conus, and the systolic murmur in the second
left intercostal space with accentuation of the pulmonary second sound are in keeping with the
diagnosis of an atrial septal defect   Left ventricular enlargement and left axis deviation are, on the
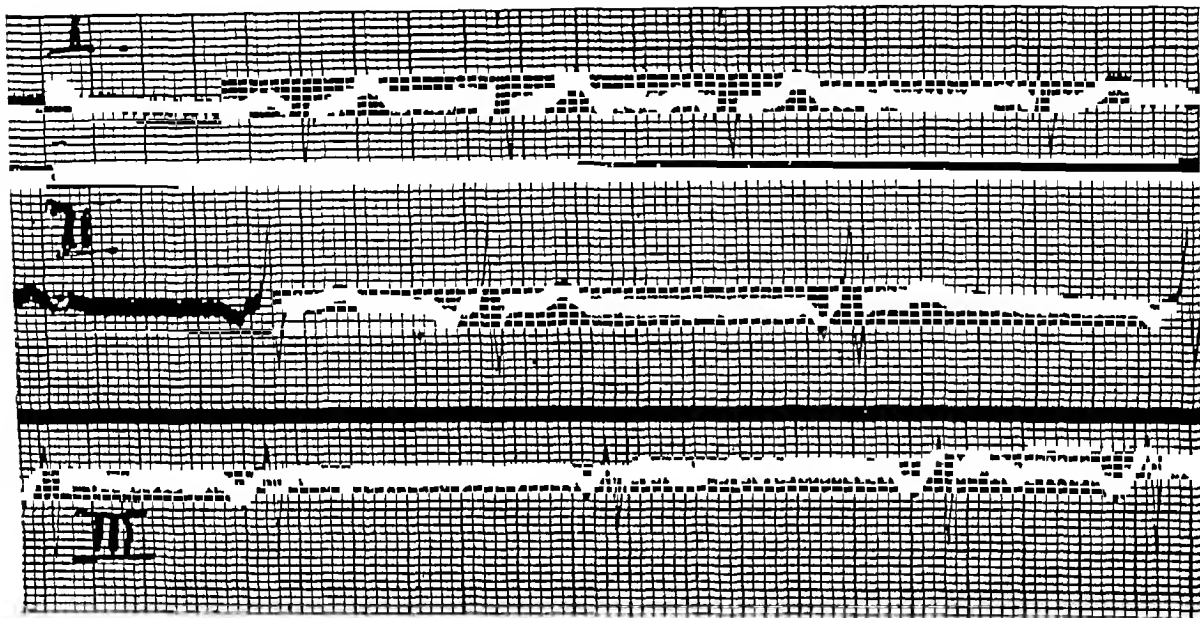
FIG 2 —Case 1 Electrocardiogram, showing sinus arrhythmia, left axis deviation, inversion of P II, P III,
and T III

other hand, exceptional   in fact enlargement of the right ventricle and right axis deviation were
found to be the rule in a series of 53 cases analysed by Bedford *et al* (1940)   A possible explanation
of the anomaly is that in this case the ventricles are transposed and that the aorta, which is displaced
towards the right, originates from an arterial right ventricle, the whole of the left border of the heart
being formed by a venous left ventricle

Some of the clinical findings, taken separately, would fit the diagnosis of pulmonary stenosis or of
patent ductus arteriosus, but the evidence as a whole is against these, and the preponderance of the
left ventricle would still remain unexplained   The most likely diagnosis is, therefore, patency of the
atrial septum with corrected transposition of the great vessels, although it must remain speculative

Case 2   A boy, aged 5 years, was admitted to the County Hospital, Farnborough, in May 1945,
suffering from intestinal obstruction   He had been deeply cyanosed from birth, and clubbing of the
fingers and toes had been present since early childhood   His capacity for exercise had always been
much below normal

On laparotomy he was found to have an ileo-cæcal intussusception, associated with non-rotation
of the mid-gut   The cæcum was under the liver in the left upper compartment of the abdomen and the
rest of the large intestine was displaced into the right half of the peritoneal cavity   The stomach
was displaced to the right, and, as a later barium meal (Fig 3) showed, its position was a mirror

image of the normal   Further details of the disposition of the abdominal viscera were published by van Meurs (1946)

The heart was moderately enlarged, with the apex beat 2 cm outside the mid-clavicular line, and a strip of dullness for a distance of 1 5 cm to the right of the sternum   A loud, rasping systolic murmur was heard over a wide area of the præcordium, with its maximum intensity in the third left intercostal space   The blood pressure was 90/60   The red cell count was 8 1 million with the hæmoglobin 130 per cent

FIG 3 —Case 2   Barium meal, showing reversed   FIG 4 —Case 2 Postero-anterior teleradiogram Cœur
        position of the stomach and jejunum   en sabot   Displacement of the aorta to the right
                                                                  Double aortic arch

X-ray findings   (Fig 4)   The heart was moderately enlarged with a maximum transverse diameter of 11 5 cm   It was slightly displaced to the right   the right border of the ascending aorta was 4 5 cm from the mid-line and part of the aortic arch appeared to the right of the trachea   1 5 cm higher, to the left of the trachea, there was another semicircular shadow, which possibly represented a second aortic arch

Diagnosis   The deep cyanosis dating back to birth, with polycythæmia and clubbing of the fingers, is evidence of a congenital cardiac defect, with free mixing of blood between the right and left chambers   In view of the shape of the heart the displacement of the aorta towards the right, and the loud systolic murmur in the third left intercostal space, the diagnosis of Fallot's tetralogy is highly probable

SUMMARY OF REPORTED CASES AND DISCUSSION

A search produced only 12 further reported cases of congenital heart disease associated with isolated inversion of the abdominal viscera   Details of these are shown in Table I

It would be unwise in this small series of cases to base an estimate of the total incidence

TABLE I

Author	Age and Sex	Type of Heart Disease	Abdominal Viscera	Autopsy
Breschet (1826) quoted by Gruber	6 weeks, M	Cor biloculare	Stomach on the right Liver central	Yes
Hickman (1869)	6 weeks, M	Atria transposed Corrected transposition of the arterial trunks Patent atrial septum Patent ventricular septum Patent ductus arteriosus	Transposed	Yes
Marchand (1883) quoted by Gruber	1 day, ?	Cor triloculare biventriculare	Stomach on the right Liver on the right	Yes
Griffith (1897) quoted by Licht-man	9 months, M	Atria transposed Transposition of the arterial trunks Patent ventricular septum Patent ductus arteriosus Pulmonary stenosis	Transposed	Yes
Lochte (1898)	17 years, M	Atria transposed Transposition of the arterial trunks Patent atrial septum Patent ventricular septum Pulmonary stenosis	Stomach on the right Liver central The left lobe larger than the right lobe	Yes
Geipel (1899) quoted by Schelenz	Unknown	Atria transposed Aorta and pulmonary artery originate from the right ventricle	Stomach on the right Liver on the right	Yes
Hingst (1901) quoted by Schelenz	Unknown	Patent atrial septum Patent ventricular septum	Spleen, liver, and stomach on the right	Yes
McCrae (1905)	49 days, M	Atria transposed Patent atrial septum Patent ductus arteriosus Pulmonary atresia	Transposed	Yes
Royer and Wilson (1908)	6½ years, M	Atria transposed Patent atrial septum Patent ventricular septum	Transposed	Yes
Knape (1912)	8 days, M	Cor triloculare biatrium Atrial septal defect Pulmonary atresia Patent ductus arteriosus	Transposed	Yes
Shaw and Blake (1924)	2 years, M	Patent ventricular septum	Transposed	No
Miller (1925)	10 weeks, F	Atria transposed Patent atrial septum Patent ductus arteriosus Pulmonary artery and aorta arise from left ventricle	Transposed	Yes

of congenital heart disease, or of the relative frequency of the various types of cardiac defect in isolated inversion of the abdominal viscera   Although there are numerous surgical reports of transposition of the abdominal organs, the heart in these cases has not, as a rule, been examined with sufficient care to reveal minor abnormalities   Also, in the days before radiological study of heart disease was adopted, the abnormal position of the stomach is likely to have been often overlooked   For this reason, the prevalence of post-mortem records of severe heart lesions in this series may well give an unduly gloomy impression of this condition

The prevalence of transposition of the atria is, however, very striking   Out of the 14 cases (including the 2 here reported) this otherwise rare abnormality was present in 8 cases   2 of the remaining 6 had a common atrium supplying both ventricles, and in 4 the disposition of the atria could not be ascertained   It appears probable that this abnormality constitutes the key defect of the heart, the associated structural changes merely serving to direct the arterial and venous return to the heart into their correct outflow channels   Of the mechanisms by which this might be achieved, transposition of the aorta into the right ventricle and of the pulmonary artery into the left ventricle is alone completely effective   All other types of defect, such as patency of the septa or of the ductus arteriosus, merely provide for admixture of arterial to the venous blood of the systemic outflow, and are, therefore, incompatible with prolonged survival   In effect, in the whole series only two cases survived to adult age (Lochte, 17 years, and Forgacs, 26 years), in these subjects corrected transposition of the arterial trunks was diagnosed by post-mortem examination in the first, and on clinical grounds in the second   Of the remaining 12 cases, 6 died in the first few weeks of life and none of the others was over the age of seven at the time of observation

The remarkable prevalence of transposition of the atria may offer a clue to the pathogenesis of the congenital heart lesions in this group and also in the very similar group of isolated dextrocardia   This type of heterotaxy, which is the exact reverse of the visceral arrangement under discussion, is nearly always complicated by congenital malformations of the heart   Lichtman (1931), in his survey of 161 reported cases of isolated dextrocardia, found only 3 examples of anatomically normal hearts   An interesting and significant fact emerges from Roesler's (1930) detailed analysis of 24 cases of isolated dextrocardia   the inferior vena cava terminated in the right atrium in 16 of the 18 in which the relevant data were available

In an ideal mirror picture dextrocardia the vena cava runs into the left atrium, an arrangement which is the rule when both the heart and the abdominal viscera are transposed   In this group, as is well known, the heart is nearly always free from structural defect   If we accept such cases as the standard of the normal right-sided heart, it will be apparent that in Roesler's series the position of the atria is reversed   It may be stated, therefore, that when the abdominal viscera alone or the heart alone is transposed to the opposite side of the body, the arrangement of the atria is usually the reverse of the normal

The similarity between the two groups of cases suggests a common pathogenesis of the cardiac defects   Of the many explanations put forward to account for the malformation of the heart in isolated dextrocardia, those which explain it as a result of torsion (Pal, 1907) or those which assume the heart lesions to be primary and the transposition of the heart as an effect of these (Monckeberg, 1915) are clearly not applicable to isolated transposition of the abdominal viscera, in which the heart remains in its normal position   A satisfactory hypothesis, valid for both groups, must take into account the abnormal relative position of the abdominal viscera and the heart   The only conceivable mechanism by which the position of the abdominal organs might influence the structure of the heart is through the agency of the embryonic abdominal venous channels

To make the argument clearer, it is useful to recall that the original symmetry of the

sinus venosus of the embryo is later destroyed by the disproportionately rapid increase in size of the right horn of the sinus   This structure is subsequently incorporated into the primitive atrium and eventually forms part of the right atrium of the mature fœtus   The rapid growth of the right horn of the sinus is determined by the development of transverse anastomoses in the abdominal venous channels shunting blood from the left side of the abdomen to the veins on the right, which terminate in the right horn of the sinus   Finally the veins on the left disappear, and the whole of the inflow from the liver and the placenta is delivered into the right atrium by way of the vena hepatis communis   This vein is later incorporated into, and forms, the terminal portion of the inferior vena cava

It is clear, therefore, that the abdomina venous channels of the embryo have a profound influence in determining the development of the atria   It seems probable that the reversal of the normal relationship between the heart and the liver in the two varieties of incomplete heterotaxy is associated with a corresponding change in the hepatic venous channels, a possibility discussed in detail by Lochte (1898)   In the event of such a change the " left " horn of the sinus venosus would receive the venous return from the liver and placenta, and in the course of embryonic development, the inferior vena cava would come to terminate in the " left " atrium

The transposition of the atria, which may be regarded as the fundamental defect in most cases of isolated inversion of the abdominal viscera and of isolated dextrocardia, is then a necessary sequel of the reversed connection between the abdominal veins and the sinus venosus   The associated malformations of the heart occur, as already suggested, as a result of the faulty development of the cardiac septa, or of an incomplete torsion of the aorto-pulmonary septum, in an attempt to divert the venous return into its correct outflow channel

SUMMARY

Two cases of congenital heart disease associated with isolated inversion of the abdominal viscera are described, together with a summary of similar cases that have been reported

An attempt is made to correlate the findings in this group with those in isolated dextrocardia

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SUBACUTE BACTERIAL ENDOCARDITIS WITH ONSET AS OPTIC NEURITIS

BY

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Although retinitis, optic neuritis, or " choked disc " occurring in the course of subacute bacterial endocarditis is not uncommon (Kimmelstiel, 1928), complaint of visual abnormality or the finding or papilloedema as an initial or early manifestation of the disease is not usual The two following cases presented difficulty in diagnosis by the predominantly neurological picture, emphasized by involvement of the optic nerve

Case 1 *Retrobular neuritis with subacute bacterial endocarditis*

A housewife, aged 30, was admitted to hospital with a story of increasingly misty vision in the right eye At the age of 10 she had rheumatic fever and later during convalescence involvement of the aortic valve was noted Since the birth of her first child by Caesarean section one year previously she had not felt completely well and had become easily fatigued, but there was no undue dyspnœa and she was able to swim and dance without inconvenience One month before admission she noted black spots before the right eye followed by blurring of vision There had not been limb weakness, diplopia, or abnormality in micturition

Examination showed a well-built, somewhat obese young woman There was a left internal rectus weakness (present since childhood) and blurring of the outline of the right optic disc There was no gross defect of the visual fields on confrontation and the central nervous system otherwise showed no abnormality There was a " collapsing " pulse, cardiac enlargement to the left with impulse four and three-quarter inches from the mid-line in the fifth left interspace, and aortic diastolic and systolic bruits The blood pressure was 165/60 There were no signs of cardiac failure, except that the liver edge was palpable and tender one finger's breadth below the right costal margin The cerebrospinal fluid at an initial pressure of 230 mm was otherwise normal The Wassermann reaction in the blood and C S F was negative The blood sedimentation rate was 6 mm in the first hour The urine was normal clinically and microscopically

On X-ray screening there was enlargement of the left ventricle An electrocardiogram showed splintering of R III, depression of S–T II, and inversion of T II and T III

During one week in hospital there was no fever The patient was discharged with a diagnosis of retrobulbar neuritis and rheumatic carditis (aortic reflux)

Eight months later she was again admitted to hospital The amblyopia had disappeared within a month of her previous admission and for four months she had remained in fair health, until following a dental abscess she complained of headache, sweats, and increasing lassitude There had been irregular fever, usually in the afternoon nevertheless she continued at her household duties For two days before admission she had noted painful spots in the palms of the hands

Clinical examination showed a temperature of 101° F , two Osler's nodes in the palm of the right hand, and two petechiæ over the right shin There was no finger *clubbing* Apart from tachycardia the cardiovascular signs (cardiac enlargement with aortic reflux) remained unchanged The liver was no longer palpable but the spleen was now one finger's breadth

below the costal margin   There was some pallor of the right optic disc and a small hæmorrhage in the right optic fundus, there were no other abnormal neurological findings

Blood culture on three successive days grew *Streptococcus viridans* (penicillin sensitive) The red blood corpuscles were 4,100,000, the hæmoglobin 80 per cent, the white blood corpuscles were 9,600—polymorphs 73 per cent, lymphocytes 23 per cent, and mononuclears 4 per cent

The urinary deposit showed red blood cells

For the four days prior to treatment with penicillin the temperature was of the picket fence type   The fever responded to penicillin within twenty-four hours but during the first week of treatment a splenic infarct occurred and Osler's nodes appeared at intervals   In the
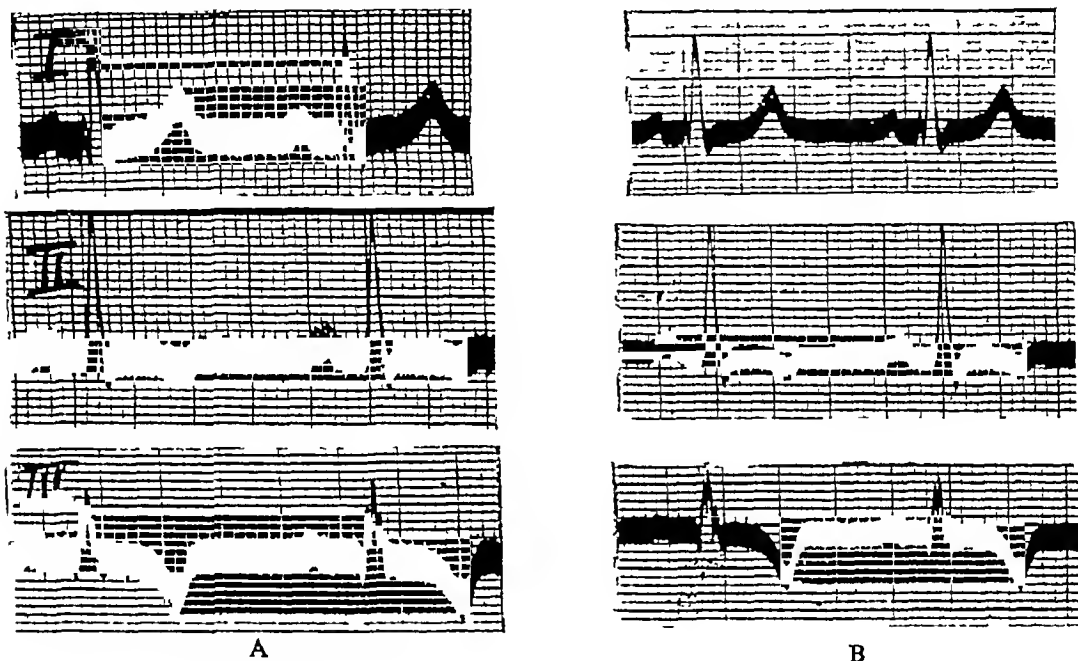
FIG 1 —Electrocardiograms of Case 1   (A) During the retrobulbar neuritis   (B) One year later when symptom free

third week of treatment there was sudden onset of motor aphasia (the B S R at this time was 3 mm)   The total dosage of penicillin was seven million units over 30 days   Before discharge from hospital repeated blood cultures were sterile

Three months later she reported herself as well, and the speech was normal except for an occasional hesitancy

Comment   Presumably the retrobulbar neuritis was of embolic origin although examination at the time did not suggest any such dramatic event

It is tempting to interpret the changes in the cardiogram (Fig 1) as the result of a posterior infarction , however, there is nothing to substantiate this clinically and serial cardiograms over a period of a year have shown little change in the contours, so that the aortic reflux alone is the likely cause of this ischæmic posterior coronary pattern

The peculiar interest of the case is the unusual neurological presentation of subacute bacterial endocarditis and the lengthy latent period before general signs became apparent At her first admission the retrobulbar neuritis was considered of the usual unknown ætiology there being no other embolic or toxæmic manifestation   Perhaps the onset of the disease, as evidenced by undue fatigue, dates from the birth of her child some sixteen months before frank symptoms, alternatively it may be suggested that the bacterial endocarditis dates only from

the dental abscess which would entail a second pathology for the retrobulbar neuritis, a less attractive supposition

Case 2 Subacute bacterial endocarditis with papilloedema, mimicking intracranial tumour

A married woman, aged 25, was admitted to hospital with a history of left hemiplegia of sudden onset At the age of ten she had rheumatic fever which left in its train a heart murmur

One week before admission there was severe epigastric pain followed two days later by numbness of the left side of the mouth, and the next morning she discovered her left side paralysed and anæsthetic Eighteen months previously and coincident with the first pregnancy, she noted generalized vertical headaches, these were less evident after a miscarriage at ten weeks Two months before admission, when she was again pregnant, she experienced troublesome right occipital headaches for two weeks, which recurred with the onset of the hemiplegia One month ago there had been sudden pain in the left lower jaw with trismus lasting for a week There had recently been some deterioration in vision

Physical examination showed a left hemiplegia with maximum weakness in the left arm The tendon reflexes were sluggish, there were a left Babinski, left hypoæsthesia, and a dis-ordered response to pinprick on the left side There was bilateral papilloedema, more marked on the left, with great engorgement of the retinal veins There was no aphasia

The temperature was normal, the heart was not apparently enlarged, rate, rhythm, and sounds were normal, at the apex there was a blowing systolic murmur The blood pressure was 120/90 She was eight weeks pregnant

There was a tender swelling over the horizontal ramus of the left mandible without obvious dental cause, and radiographs of the mandible showed no abnormality

The urine at first showed no abnormality but later there were occasional granular casts and a few red cells The hæmoglobin was 70 per cent, the red cells 4,450,000, and the white cells 16,000 with 84 per cent polymorphs The blood sedimentation rate was 60 mm in the first hour Repeated blood cultures were sterile

The headache and papilloedema increased , vomiting later became frequent A month after admission she suddenly complained of paræsthesiæ in the left hand with motor aphasia accompanied by an indescribable mental state, all of short duration Ventriculography showed no abnormality After three months of progressive deterioration the illness ended in bronchopneumonia The temperature apart from an occasional rise to 99° to 100° F at noon had shown little abnormal until the pre-terminal fever

Autopsy This revealed a small yellow area of necrosis in the posterior limb of the right internal capsule encroaching on the optic thalamus, a more recent infarct one inch in diameter in the right occipital lobe, and the most recent lesion two inches in diameter in the left parietal lobe

The heart showed moderate dilatation of all its chambers There was thickening and distortion of the anterior cusp of the mitral valve but there was no true stenosis Mural endocarditis was present on the posterior wall of the left auricle There were old infarctions in both kidneys and there was a single infarct in the spleen The liver was enlarged and congested

There were pleural adhesions over the right lung and early bronchopneumonia was present The uterus contained a healthy male fœtus of 4 to 5 months

Comment Here the antecedent period before gross embolic manifestation was probably eighteen months At admission the picture was so dominated by the " choked discs " that the tentative diagnosis was intracranial tumour, in support of which were the progressive nature of the papilloedema and later vomiting The possibility of bacterial endocarditis was entertained, but repeatedly negative blood cultures and the absence of fever, of splenomegaly, and of skin emboli obscured the true aetiology of the neurological findings The presence of an old rheumatic valvular lesion was of paramount diagnostic significance

Discussion

Over an eight-year period there were 26 patients admitted to St George's Hospital who showed unequivocal evidence of subacute bacterial endocarditis   Among these were 5 patients in whom note of ocular symptoms was made , 3 showed hæmorrhage into the fundus oculi and the 2 with involvement of the optic nerve are here recorded   Krinsky and Merritt (1938) considered that 20 of their series of 100 cases of bacterial endocarditis showed a picture so predominantly neurological that the primary lesion was thought to lie in the central nervous system   They noted that 10 per cent of patients complained of visual disturbance at some stage of the disease, compared with headache the most common neurological symptom, which occurred in 24 per cent , " choked discs " were observed in 8 per cent   They describe a slowly developing hemiplegia with mixed aphasia and left hypoalgesia in a left-handed male where progressive papillœdema appeared to support the diagnosis of tumour , later fever, petechiæ, valvular involvement, and a positive blood culture established the true ætiology In a further patient amblyopia had occurred some months before admission with hemiplegia, the result of endocarditis lenta

As embolism is the essential feature of the symptomatology of subacute bacterial endocarditis and as death from cerebral embolism occurs in 23 per cent (Blumer, 1923), it is surprising that bizarre neurological and psychiatric complications are not more common   Kernohan et al (1939) report that in every case of subacute bacterial endocarditis in which they examined the brain microscopically, widespread reactions associated with occluded arterioles or capillaries were found   The lesions were the result either of embolism, in which the endothelium of the intima surrounded the blood clot, or of thrombosis in situ, in which the initial lesion consisted of a hyaline change in the vessel wall progressing to partial occlusion of the lumen and here endothelial cells were present in the middle of hyaline thrombus   These latter changes they attribute to cocci or the local effect or their toxins

Changes in the optic nerve are the result of occlusion in part of the blood supply, which gives rise to swelling of the nerve, lying for most of its course in the unyielding surroundings of the optic foramen   It is, therefore, a matter of the degree of occlusion and subsequent swelling whether retrobulbar neuritis with slight blurring of the disc outline or gross papillœdema with obstruction of the retinal veins occurs   Spread of intravascular clotting or repeated embolism is presumably the cause of the progressive nature of the papillœdema, which seems to be characteristic   Theoretically there is no reason why the choked disc should not be unilateral, although it is probable that where repeated embolism has occurred in one optic nerve the other nerve is unlikely to remain unscathed

The practical conclusion from the reported cases is that where rheumatic or congenital heart disease exists in the presence of neurological findings, particularly where these are of sudden onset, endocarditis lenta is a very real possibility, the absence of other contributory evidence is not exclusive of this diagnosis

Summary

Two cases of subacute bacterial endocarditis with early involvement of the optic nerve are described and the difficulty in diagnosis emphasized   Neurological presentation of the disease is not uncommon, and optic neuritis, even of a progressive nature, is not an incompatible finding

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PENICILLIN TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS

BY

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The early impression that penicillin was ineffective in subacute bacterial endocarditis arose from the first case treated, that of Florey and Florey (1943), and from the 17 cases unsuccessfully treated by Keefer *et al* (1943) In the following year Loewe *et al* (1944) recorded 7 apparently successful cases, but the period of observation was very short More failures followed (Herrell, 1944, Herrell *et al*, 1944, Bloomfield *et al*, 1944), but Dawson and Hobby

TABLE I

CASES OF SUBACUTE BACTERIAL ENDOCARDITIS TREATED WITH PENICILLIN REPORTED BETWEEN
JANUARY 1945 AND AUGUST 1946

Reference	Number of cases	Number of cases alive and free from infection	Period of observation after treatment (months)
Bloomfield, Armstrong, and Kirby (1945)	11*	9	1–6
Bloomfield and Halpern (1945)	18†	18	3–17
Christie (1946)	147‡	81	3–8
Dawson and Hunter (1946)	35§	30	3–32
Favour, Janeway, Gibson, and Levine (1946)	17	11	6–18
Flippin, Mayock, Murphy, and Wolferth (1945)	20	12	2–17
Glaser, Smith, Harford, and Wood (1946)	22	13	1–24
Goerner, Geiger, and Blake (1945)	16	11	3–13
Levy and McKrill (1946)	11	6	11–18
Loewe (1945)	54	37	2–15
Meads, Harris, and Finland (1945)	9	7	1–11
Mokotoff, Brams, Katz, and Howell (1946)	17	13	8–20
White, Mathews, and Evans (1945)	9	6	2–8
Various —Anderson and Keefer (1945), Geiger and Goerner (1946), Hines and Kessler (1945), Kelson (1945), Paullin and McLoughlin (1945), Russek *et al* (1945), Vesell and Kross (1946)	20	12	various
Totals	406	266	

* Favourable cases selected, with 3 exceptions
† Favourable cases selected, an unstated number previously reported were included
‡ Collected British cases including 18 cases of Ward, Meanock, Selbie, and Simon (1946) and 20 cases of Sanderson and McEntegart (1946)
§ First 5 cases selected as favourable, and 30 unselected except organism penicillin-sensitive

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(1944) were successful in 3 of 10 cases   At this time Keefer (1944) stated that of 55 cases treated in the United States only 3 were alive a year later

By 1945 it was realized that to be successful penicillin must be administered in large doses for long periods, Keefer (1945) suggested 200,000 to 300,000 units daily for 3 weeks, Loewe (1945) advised up to 1,000,000 units daily for 5 weeks and Bloomfield et al (1945) gave 200,000 units daily for 6 to 8 weeks   The subsequent results have been considerably better and, since the beginning of 1945, reports of 406 cases with 266 recoveries have been published in this country and in the United States, these are summarized in Table I   In some instances the results are not representative of the value of penicillin in unselected cases for, owing to shortage of penicillin at the time, those likely to benefit from treatment were chosen

Early in 1945 the Medical Research Council initiated a coordinated investigation at 12 centres in Britain, and Christie (1946) has published a summary of the results in the first 147 unselected cases with 81 recoveries   At the Manchester centre 40 have so far been treated, 7 of these, in which treatment was completed less than six months ago, are excluded   This period has been selected because in published cases, death has so far not occurred more than six months after successful treatment except from heart failure or unrelated causes   Only those in which the causative organism was isolated are included, but otherwise there has been no selection , 2 patients were moribund on admission and in 1 the infecting organism was insensitive to penicillin

SOME CLINICAL FEATURES BEFORE TREATMENT

Of 33 patients, 11 were male and 22 female, their ages ranged from 13 to 59
Capacity for Effort before Infection   Subacute bacterial endocarditis rarely develops when rheumatic or congenital heart disease is severe (Libman and Friedberg, 1942), none of our patients had auricular fibrillation or a history of heart failure prior to infection and all were either in employment or looked after their homes and families or studied at school or college (Table II)   In only 3 cases had there been considerable impairment of capacity for effort

TABLE II

CAPACITY FOR EFFORT AND OCCUPATION BEFORE INFECTION

Capacity for effort	Number of cases	Sedentary employment	Non-sedentary employment	Housework	School or college
Class I	17	4	7	4	2
Class II	13	2	4	7	—
Class III	3	1	—	2	—
Totals	33	7	11	13	2

before infection (Class III), in 13 cases some dyspnoea had occurred on unusual exertion but not during ordinary activity (Class II), in 17 cases no symptoms had been noticed on exertion and 8 of these patients had been unaware of their cardiac lesion (Class I)   The classification used in that accepted by the American Heart Association (*Criteria for Nomenclature and Diagnosis*, 1942)

Physical Signs of Underlying Heart Disease   Rheumatic heart disease was present in 28 and congenital heart disease in 4 cases, in one both congenital and rheumatic lesions were found at necropsy   In 11 of our 29 rheumatic cases only systolic murmurs were present on admission and we have been impressed by the rarity of the typical presystolic murmur when

bacterial endocarditis is present   Although radioscopy sometimes showed pulmonary congestion and enlargement of the right ventricle consistent with well-developed mitral stenosis, we believe that the rarity of the characteristic physical signs is principally because only slight mitral lesions were present in most cases, for mitral stenosis was present in only 2 of 12 cases with rheumatic heart disease that came to necropsy   Aortic incompetence, however, appeared to be disproportionately common, for it was present clinically in 16 of 29 rheumatic cases   This high proportion may be due to the tendency for subacute bacterial endocarditis to attack the aortic valve, so that some aortic lesions may have arisen from the infection and not from the underlying rheumatic heart disease

Thus, in this series, both the good capacity for effort before infection and the nature of the rheumatic valvular lesions support the view that the underlying heart disease was usually relatively slight

The Onset of Bacterial Endocarditis   This occurred during pregnancy or at confinement in 7 cases, nearly one-third of our female cases   In 3 cases symptoms of infection were first noticed, two, six, and nine weeks after dental extractions

The initial symptoms of bacterial endocarditis rarely give any indication of the nature of the infection (Christian, 1941), in our cases the commonest presenting features were lassitude (10 cases), generalized " rheumatic " pains (6), pyrexia in patients already under observation (6), or a vague illness resembling influenza (5 cases)   In 3 cases major embolic accidents marked the onset of symptoms, in one a subarachnoid hæmorrhage was presumably due to rupture of a mycotic cerebral aneurysm, in a second hæmoptysis from a pulmonary infarct led to a mistaken diagnosis of pulmonary tuberculosis, and in the third visible hæmaturia and loin pain from a large renal infarct suggested the presence of a urinary calculus   Persistent sweating (twice) and pallor (once) were the presenting symptoms in the other 3 cases

The subsequent symptoms were protean   Loss of weight occurred in every case but was often not noticed until several months after the onset of the infection   Generalized " rheumatic " pains developed at some stage in 17 cases   These pains were sudden in onset but fleeting in character, they were rarely confined to the joints but often affected muscle masses in the limbs or trunk   They sometimes led to a mistaken diagnosis of " rheumatism " or rheumatic fever   Pain persisting in one site, presumably embolic in origin, was noticed in 21 cases, in 9 in a limb, in 5 in the splenic area, in 4 in the chest, in 2 in the lumbar area and in 1 severe central abdominal pain persisted for several weeks   Nausea and vomiting were common, and persistent sweating was noticed in 15 and rigors in 4 cases   Progressive impairment of capacity for effort was a feature in 16 and was followed by heart failure in 15, this was usually a late feature of cases in which the diagnosis was delayed

In over one-third of our cases (13) symptoms had been present for twenty or more weeks before treatment

In addition to the 3 cases in which symptoms of bacterial endocarditis followed dental extraction, teeth were extracted after the onset of bacterial endocarditis in 2 others, and paradontal sepsis was present in 9 others   Tonsillar sepsis was found in 4 and cholecystitis in 1 case   The frequency of paradontal and tonsillar sepsis in this series supports the suggestion that the mouth and pharynx are often the sites from which the cardiac infection arises but, since *Strept viridans* can be grown from the normal mouth, it did not seem worthwhile to attempt to compare the organism grown from the blood with the flora of the mouth and pharynx

Sulphonamides had been given to 15 cases before admission, in all these the causative organism was subsequently isolated from the blood

INVESTIGATIONS

The scheme of investigation is detailed in Table III

Blood Cultures were made without regard to the temperature of the patient by the method of Penfold, Goldman, and Fairbrother (1940)   7 c c of blood was withdrawn from a vein into a sterile oil-free syringe, 2 c c was introduced into a small vial containing a balanced oxalate mixture (Wintrobe and Landsberg, 1935) and reserved for the erythrocyte sedimentation rate, 1 c c was added to 4 c c glucose trypsin broth and 1 c c to 4 c c saponin broth, with these pour plates were made using melted agar   The remaining 3 c c was added to 50 c c of Hartley digest broth   The inoculated media were incubated at 37° C under atmospheric conditions and kept 14 days before a final negative report was given   If negative, further cultures were incubated in an atmosphere of 10 per cent CO_2 as it was found that several strains grew more readily, or could only be grown, under these conditions this technique was later adopted in all cases   To cultures taken during penicillin therapy sufficient penicillinase (prepared by the method of Duthie, 1944) was added to neutralize a concentration of at least 10 units of penicillin per c c of blood

TABLE III

SCHEME OF INVESTIGATION

Before treatment	During treatment	After treatment
Cardioscopy Cardiogram	Cardioscopy Cardiogram } At end of treatment	Cardioscopy Cardiogram } At intervals
Blood culture Full blood count Sedimentation rate Microscopy urinary deposit	Blood culture Hæmoglobin and total white count Sedimentation rate Microscopy urinary deposit } Weekly	Blood culture Hæmoglobin and total white count Sedimentation rate Microscopy urinary deposit } In first week, every two weeks in hospital, if apyrexial, monthly after discharge
Urea clearance Blood urea Bacteriology of urine	Urea clearance Blood urea } If indicated Serum penicillin levels (three times weekly)	Urea clearance Blood urea } If previously abnormal

In 16 of 33 cases positive blood cultures had been obtained before admission, in 5 repeated cultures had been negative, and in 12 no culture had been attempted   On admission a positive culture was obtained at the first attempt in 29 and on the second attempt in the remaining 4 cases   In only one, admitted with suspected bacterial endocarditis during this investigation, were we unable to isolate an organism, that case is, therefore, not included in this series   Using the technique we have described it is rare to encounter difficulty in isolating the organism in clinical cases of bacterial endocarditis

Strept viridans was isolated in 26 and non-hæmolytic streptococci in 5 cases, in 1 of the remaining 2 the organism was *Hæmophilus influenzæ* and in the other case a *Pneumococcus* was isolated

TABLE IV

COEFFICIENTS OF RESISTANCE OF INFECTING ORGANISMS

Organism	Number of cases	Coefficient of resistance		
		<0 5	0 5–4 0	>4 0
Streptococcus viridans	26	6	18	2
Non-hæmolytic streptococcus	5	3	2	—
Hæmophilus influenzæ	1	—	—	1
Pneumococcus	1	Not tested quantitatively		

Coefficients of Resistance of the Organisms   Two sets of tubes were prepared with twofold decreasing dilutions of a nutrient broth containing a known concentration of penicillin   Each tube of one set was inoculated with a standard drop of a 24-hour broth culture of *Staph pyogenes* (Oxford " H " strain) and to each tube of the other set a drop of a broth suspension of the test organism was added   All tubes were incubated overnight and the resistance of the organism to penicillin estimated by comparing the concentration of penicillin necessary to inhibit its growth with the concentration that inhibited growth of the Oxford staphylococcus, the resistance of the test organism was expressed as a multiple of the resistance of the Oxford staphylococcus   Our observations are summarized in Table IV

Penicillin Serum Levels   The penicillin level in the blood was estimated in a similar way, but in one set of tubes the patient's serum was used instead of the penicillin solution and all tubes were inoculated with the Oxford staphylococcus   The bacteriostatic activity of the patient's serum was thus compared with that of known concentrations of penicillin

These methods of estimating the resistance of the organism and the penicillin serum level are open to criticism   Although standard solutions of penicillin do not contain less than the stated amount, they may contain rather more and this will lead to an underestimate of the penicillin serum level   The penicillin sensitivity of the Oxford staphylococcus varies in subculture and is not an altogether reliable standard for assessing the resistance of the test organism   Similar difficulties have been encountered by Glaser *et al* (1946)   The principal value of these tests lies in their ability to recognize insensitive organisms and to indicate whether the patient's blood is bacteriostatic

Blood Counts and Sedimentation Rate   At first the sedimentation rate was estimated using a Wintrobe tube, later the reading was corrected by the method of Wintrobe and Landsberg (1935)   The uncorrected rate was invariably raised before treatment but, of 13 cases in which a correction from the hæmatocrit reading was applied, 1 was within normal limits and 2 were high normals (12 and 14 mm in the first hour)

In 24, the hæmoglobin on the Haldane standard was less than 70 per cent on admission and less than 50 per cent in 8 cases   On admission an increase in the number of polymorphonuclear leucocytes was found in 26, this was not always revealed by a total leucocyte count, which was increased in only 14 cases

Cardiac and Renal Investigations   There were 28 patients who were fit for 6 ft teleradiograms before treatment, in 8 the heart was not appreciably enlarged, in 13 the cardiothoracic ratio was between 1 9 and 1 6, and in 7 gross enlargement was present (cardiothoracic ratio 1 5 or less)

Cardiograms were taken before treatment in 32 cases, 13 were within normal limits, including 6 with left axis deviation and aortic incompetence   The principal abnormalities were prolonged P-R in 1, right axis deviation in 2, left ventricular strain in 9, low voltage QRS (all leads) in 2, low voltage T (all leads) in 5, right B B BI in 1, and dextrocardia in 1 case (more than one abnormality were present in 2 cases)   The infrequency of right axis deviation is further confirmation of the absence of severe mitral lesions in these cases

We have accepted as abnormal a blood urea of more than 40 mg per 100 c c and a standard urea clearance of less than 70 per cent   When the urinary deposit contained a few red cells with, usually, a few leucocytes and granular and cellular casts, we have classified the abnormality as " slight," whereas when many red cells were visible as a naked-eye deposit, usually accompanied by many leucocytes and casts, we have described the abnormality as " gross "   By these criteria, the renal function was impaired in 10 cases, whereas the urinary deposit was always abnormal, the changes being " slight " in 19 and " gross " in 14 cases

TREATMENT

Apart from the treatment of heart failure, of anæmia, and of focal sepsis, the only therapeutic measure used in these cases was the administration of penicillin

At first various schemes were adopted to determine the duration of treatment and the dosage of penicillin necessary to control the infection, these experiments were conducted at all centres and the results have been summarized by Christie (1946)   The most satisfactory course for initial treatment was 0 5 mega unit daily for 28 days   Since relapses in some of

the earlier cases were subsequently treated by a full course, and because the 28-day course was adopted very early at this centre, it happens that, of 25 of our cases who lived to complete treatment, only 3 did not receive the full course of 0 5 mega unit (or more) daily for 28 days Of these 3, one was the first in this series and died before we adopted the longer course, one, who remains well, refused treatment after two courses of nine and ten days, and in one treatment had to be stopped after three weeks owing to severe thrombopenia, this patient died four weeks later from heart failure with her infection apparently controlled   Treatment known to be inadequate does not, therefore, play an important part in assessing the results in these cases

Penicillin is remarkably free from undesirable toxic effects but, in this series, the need to give large doses for several weeks afforded a useful opportunity to study such effects   In the earlier cases we noticed that, although the temperature rapidly became normal after starting treatment, it often rose again at the beginning of the second week and an intermittent pyrexia persisted until penicillin therapy ended (Fig 1, Case 24)   During the fourth week of therapy
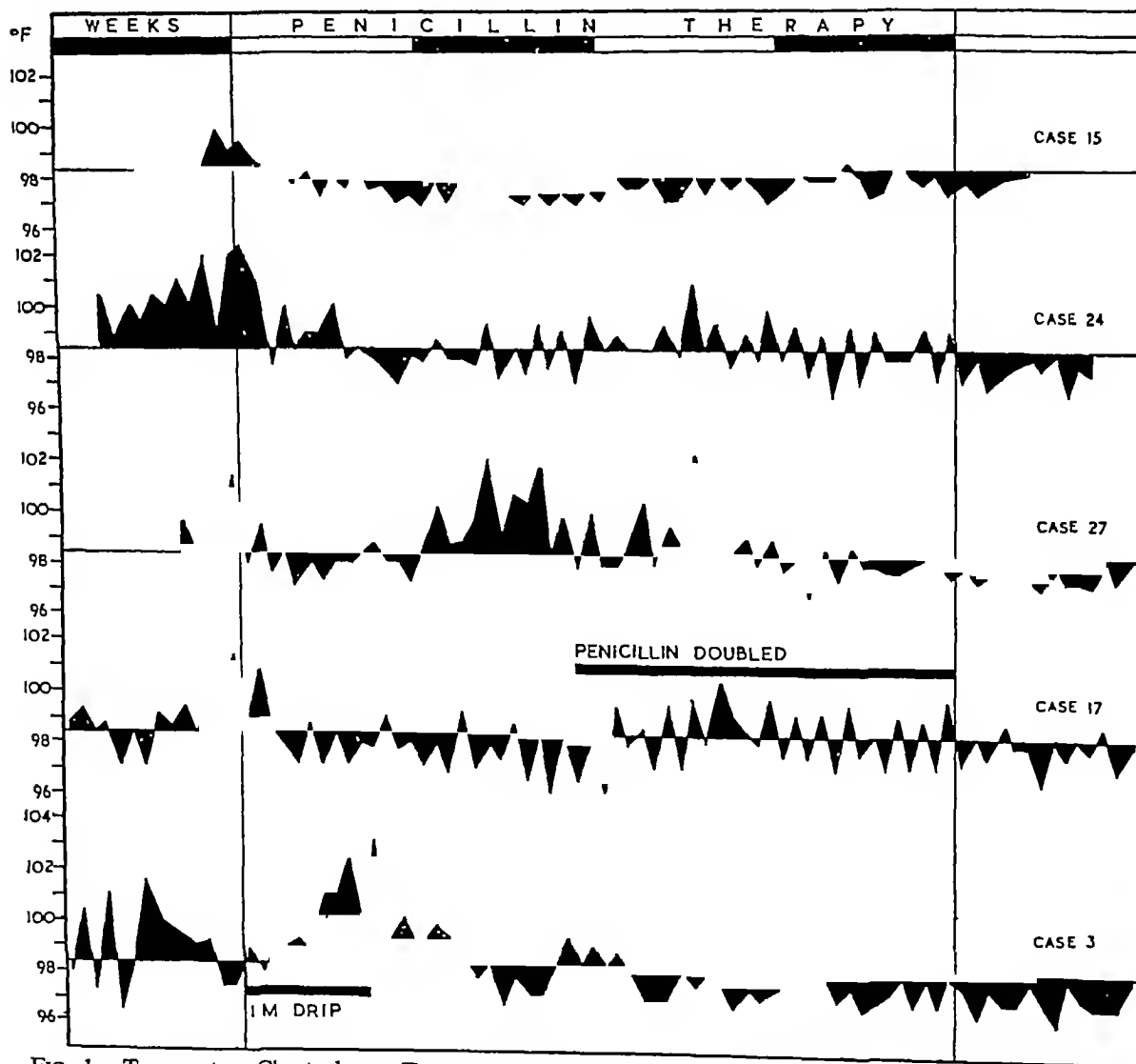
FIG 1 —Temperature Charts during Treatment   Case 15   Uncomplicated response—apyrexial after first two days   Cases 24, 27, and 17   Penicillin pyrexia   Case 3   Pyrexia due to intramuscular drip, settling when method of administration changed to three-hourly injections

the pyrexia tended to diminish and sometimes disappeared (Fig 1, Case 27) At first we were inclined to suspect that such pyrexia was due to failure to control the infection and this led us to double the dose of penicillin in 3 cases, but the pyrexia then became more striking (Fig 1, Case 17) Pyrexia of this type was noticed in 13 cases and in every case it disappeared when penicillin was discontinued We conclude that when the temperature falls to normal in the first week, a subsequent rise in the second week, which either persists until penicillin is stopped or disappears during the fourth week of treatment, can be regarded as a drug fever More highly purified penicillin became available later but this did not reduce the incidence of penicillin pyrexia which developed in 5 of the first 17 and in 8 of the last 16 cases We are, therefore, inclined to attribute the pyrexia to penicillin itself and not to impurities Penicillin pyrexia is of no prognostic significance, for of these 13 cases only 3 died Recurrence of pyrexia during treatment has been previously recorded by Dawson and Hobby (1944), Anderson and Keefer (1945), Bloomfield and Halpern (1945), Meads et al (1945), and Bloomfield et al (1945), it has usually been attributed to emboli, infection by injections or drips, or to absorption of healing lesions, but Dawson and Hobby (1944) and Bloomfield and Halpern (1945) considered it might be due to penicillin or an associated impurity It is agreed that pyrexia during treatment does not necessarily indicate failure to control the infection

In 2 cases an urticarial rash developed during the third week of treatment and disappeared a few days after the end of treatment Urticarial rashes have been previously described by Keefer et al (1943), Bloomfield et al (1945), Mokotoff et al (1946), and Geiger and Goerner (1946) In one case bruising in several parts of the body was noticed on the fourteenth day of treatment and the platelet count was 50,000 per c mm , a week later the count had fallen to 35,000, and it seemed best to stop treatment, the count then increased slowly to 58,000 before death four weeks later In another case the platelet count was 95,000 before death on the twentieth day of treatment

We have usually given penicillin by three-hourly intramuscular injection and this has been well tolerated for long periods, only one patient refused to continue treatment for the prescribed time In 5 cases, however, we used a continuous intramuscular drip, changing the site every 24 hours, but in each case, after a few days, we were obliged to change to three-hourly injections owing to severe pain at the site of injection and the development of pyrexia (Fig 1, Case 3) In all these cases the penicillin was of the less purified type and we have not tested this method using the more highly purified preparations now available

TABLE V

AVERAGE PENICILLIN SERUM LEVELS WITH 0 5 MEGA UNIT DAILY

Time after injection	Number of cases	Penicillin serum level in units per c c				
		<1	1–3	3–5	5–10	>10
Half an hour	31	1	13	11	5	1
		<0 1	0 1–0 5	0 5–1	1–5	>5
Three hours	29	3	9	7	8	2

Penicillin serum levels were estimated half an hour and three hours after the injection All our patients received 0 5 mega unit daily and the figures given in Table V are averages of the levels reached with that dose In 2 with severe renal failure, penicillin retention led to three-hour serum levels of 12 and 8 units per c c , a similar observation was made by Sanderson and McEntegart (1946) We have not been able to correlate the penicillin level with the outcome

of treatment but the levels attained appear to be bacteriostatic for all except the most insensitive organisms (Table V)

Dental and Tonsillar Infection   On admission tonsillar sepsis was present in 4 cases, 2 of these died and in the other 2 tonsillectomy was undertaken during convalescence, 0 5 mega unit of penicillin being given daily for two days before and three days after operation   On admission there was clinical or radiographic evidence of paradontal infection in 9 cases, in 4 of these treatment was undertaken during the third or fourth weeks of penicillin therapy and in 4 with penicillin cover during convalescence, 1 patient refused dental treatment   In all 10 cases in which focal sepsis was treated under penicillin cover there was no post-operative pyrexia and blood cultures remained sterile   We now prefer to eradicate focal sepsis during penicillin treatment of the bacterial endocarditis, for reinfection is possible if septic foci are still present when penicillin is discontinued

RESULTS OF TREATMENT

Of 33 patients treated, 15 have died and 18 are alive and free from signs of infection   9 for 6 to 12 months after the completion of treatment, 7 for 12 to 18 months, and 2 for over 18 months   In discussing these results in detail it is convenient to consider separately the successful and the unsuccessful cases for different problems have been investigated in each group, in successful cases we have been interested principally in studying the response to treatment and the degree of recovery which has been achieved, whereas, in those unsuccessful cases in which death occurred from heart failure, uræmia, or vascular accidents, despite control of the infection by penicillin, we have had an opportunity of investigating the factors that prevented recovery and of assessing the extent to which healing had progressed during the interval of up to three months between arrest of the infection and death

SUCCESSFUL CASES

The events during treatment in a typical successful case are illustrated in Fig 2   The temperature fell to normal within a few days of beginning treatment but the pulse settled much less rapidly, usually the rate remained somewhat rapid for two to four weeks   In the case illustrated the patient was confined to bed for three weeks after the end of treatment although the temperature and pulse rate were normal, carefully graduated and cautiously applied bed exercises were then started but were followed by an immediate rise in the pulse rate and, when the patient was allowed up for a few minutes ten days later, the pulse rate increased to 116 a minute taking several weeks to return to normal   In this case the history of infection was comparatively short and the general condition of the patient good, but it is clear that the heart had been considerably damaged by the infection   Great care is necessary during the period of increasing activity following successful treatment, however well the patient may appear when resting in bed, similar opinions were expressed by Anderson and Keefer (1945) and Meads, Harris, and Finland (1945)

The first blood culture after beginning penicillin was made between the first and seventh days of treatment and was sterile in 16 of our 18 successful cases, in the remaining 2 blood cultures were positive on the second day but sterile on the ninth day of treatment   In successful cases, once the blood was rendered sterile, subsequent cultures were always negative during treatment, but 3 patients, who ultimately recovered, relapsed after the initial course of penicillin had been completed

In 4 successful cases cardiograms before treatment showed very low voltage T waves in all the limb leads but subsequently returned to normal (Fig 7)   T wave changes associated with heart failure were noted by Bloomfield *et al* (1945), but heart failure did not occur in our 4 cases

During and after treatment the sedimentation rate fell slowly and, in our successful cases, reached normal in an average of five weeks after the completion of treatment

There was often little rise in hæmoglobin during treatment but subsequently steady improvement took place and a normal level was attained, without transfusion, about three months after the end of treatment (Fig 3)   Transfusion was necessary in only two successful cases and is to be avoided if possible owing to its dangers when heart failure is present
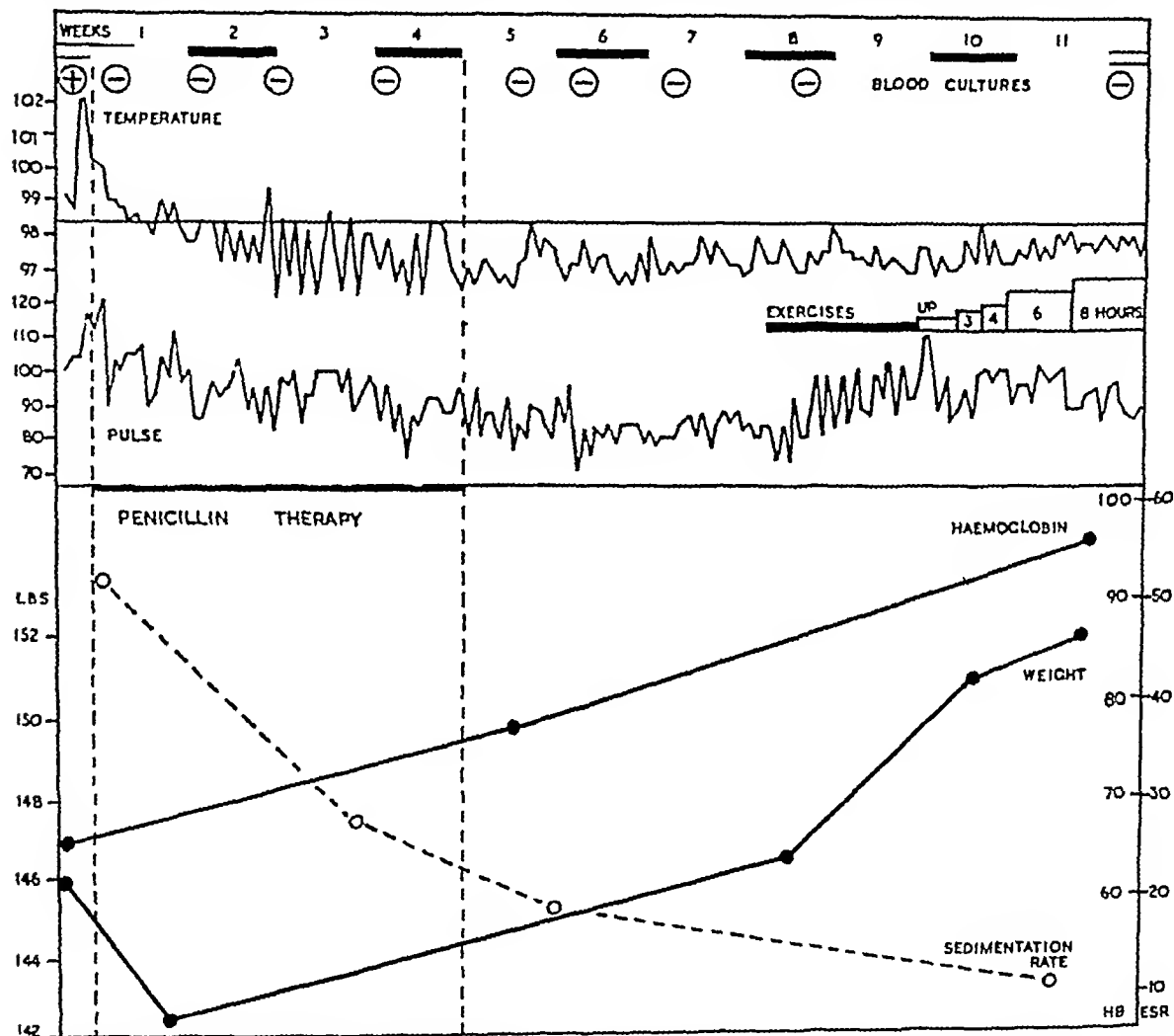
FIG 2.—Chart showing response to treatment in typical successful case   Case 13   The slow fall in pulse rate during treatment and the increase in rate on commencing activity are notable features

Gain in weight continued for up to nine months after treatment and in eight of the successful cases the gain averaged 23 lb

The convalescence of these patients was, therefore, slow and, owing to the cardiac damage, required careful management   The average period in hospital was fourteen weeks in our successful cases, full activity was rarely resumed sooner than six months after the end of treatment

Degree of Recovery

A severe infection of the myocardium and valves leading to tissue destruction and fibrosis, present for periods up to six months before arrest by penicillin, is likely to leave behind it

further cardiac damage   We have tried to assess the frequency and severity of this damage in three ways   (1) by comparing the patients' capacity for effort and ability to follow their occupation before infection and after recovery, (2) by reviewing the radioscopic changes in the size and shape of the heart and the changes in the cardiogram during the recovery stage, and (3) by searching for physical signs indicating new valvular lesions or increase in the severity of established lesions
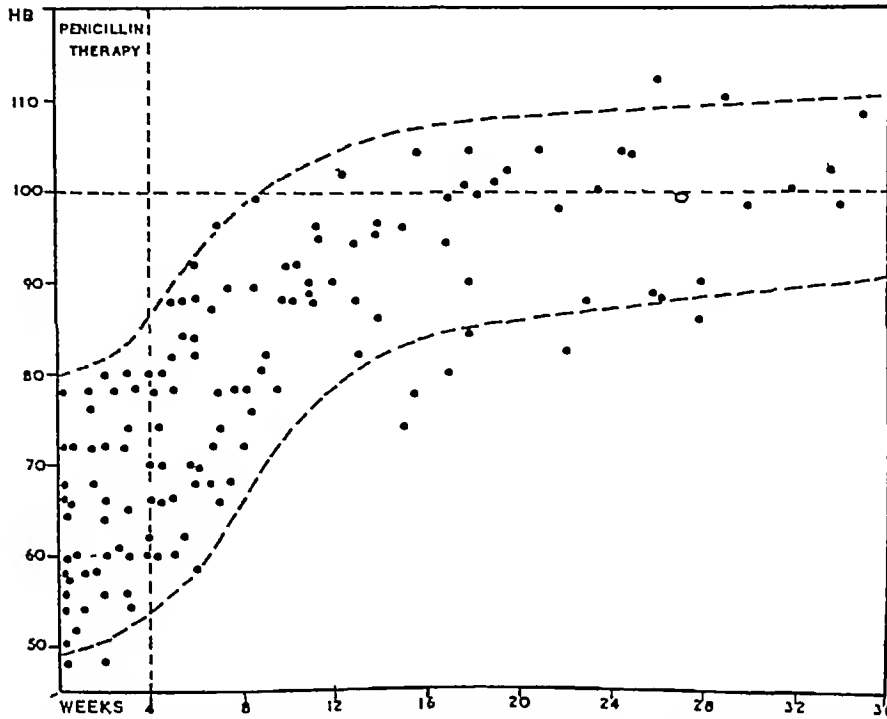
FIG   3 —Scatter graph showing rise in hæmoglobin without transfusion in 12 successful cases with an initial hæmoglobin below 80 per cent

The previous occupations of 18 recovering patients and the number who have, so far, returned to work are enumerated in Table VI   Of our 18 patients, 12 are back at their old work and all say that they notice no change in their capacity for exertion   One of these, who gave up her work as a machinist on marriage, has resumed her employment although she now has a young child born during the infection   Following that confinement she was given a ten-day course of treatment, but subsequently relapsed and, during her second course of penicillin, developed a coronary embolus with cardiographic changes indicating posterior infarction

TABLE VI

RETURN TO WORK OF 18 RECOVERING PATIENTS

Categories	Before infection	After treatment	
		Number resuming old work	Number not resuming old work
In employment	10	6	4
Housework	7	6	1
At school	1	—	1
Totals	18	12	6

One of the 6 patients who have not resumed work is still convalescent (33), one is fit for work and maintains that he is as well as before his illness but he has a specialized occupation and has not yet found suitable work   One patient had considerable restriction of her capacity for effort (Class III) before the infection, she seems no worse now but has been advised not to resume work as there is no economic necessity for her to do so   Three patients have subjectively deteriorated (10, 17, 22), and are unfit for work

The degree of recovery in these cases is surprisingly good, unfortunately, subjective estimation of fitness by the patient is open to error and objective methods reveal another aspect of the picture

Teleradiograms and Cardiograms   It is difficult to obtain strictly comparable teleradiograms for the serial measurement of heart size, we have, therefore, disregarded small changes in the cardiothoracic ratio that could be explained by a difference in position of the chest or diaphragm and have confined our attention to undoubted alterations in size

In untreated subacute bacterial endocarditis the size of the heart increases progressively as the disease advances for, in 6 of our cases, comparison of teleradiograms taken earlier in the illness with those before treatment showed that in each case the heart had increased in size, sometimes considerably (Fig 4)   After treatment there was no further increase in heart size in 13 of the 16 successful cases in which we have adequate serial teleradiograms   This suggests that, as we should expect, cardiac damage due to the infection does not often increase after successful treatment   But we have little evidence to indicate that the enlargement which occurs during the infection diminishes appreciably after apparent cure of the disease, in 9 of our 13 cases the heart size has remained unchanged for periods between six and eighteen months after treatment, and in only 4 cases has there been any suggestion of a decrease in size   In 1 of these 4, this decrease followed ligation of a patent ductus (Case 33) and is, therefore, irrelevant to this discussion, in the other 3 we are not convinced that the alteration is sufficient to be significant   Our observations, therefore, indicate that after successful treatment the progressive cardiac enlargement of the untreated disease usually stops, but enlargement that has already taken place is generally irreversible

In 3 patients cardiac enlargement continued after treatment, all these are less fit than before the infection   Case 10 is interesting for she first came under our observation when pregnant, four weeks before the first symptom of infection   She then had a loud aortic diastolic murmur, maximal to the left of the sternum and audible at the apex, with a soft systolic murmur maximal at the apex but no clear evidence of a mitral lesion   The blood pressure was 150/45   The infection was treated six weeks after the first symptom appeared and the physical signs remained unchanged   A year later a rough aortic systolic murmur and thrill appeared, but the aortic lesion remained predominantly regurgitant for the blood pressure was 135/35   Three months later a rumbling mitral diastolic murmur was heard for the first time and cardioscopy revealed increased prominence of the pulmonary conus (Fig 5) but, although the change in the valvular lesions is clinically obvious, the cardiac silhouette is not yet grossly modified and there is no significant alteration in the cardiogram   The other two cases form a striking contrast for, although the physical signs have altered much less, the heart has considerably enlarged since treatment and serial cardiograms have shown significant changes   In Case 22 the progressive increase is illustrated in Fig 6 and the development of right axis deviation in Fig 7 (A and B)   No diastolic murmur has been heard at any stage, but the apical systolic murmur is now louder   In Case 17 progressive cardiac enlargement followed the completion of treatment (Fig 8) and comparison of the cardiogram taken before treatment with that a year later showed that, in addition to recovery of the T waves previously noted, the P waves had changed and the electrical axis had shifted towards the right (Fig 7)   Although the radiograms are typical of advanced mitral stenosis there has never been a diastolic or presystolic murmur, but the apical systolic murmur has become much louder   In these
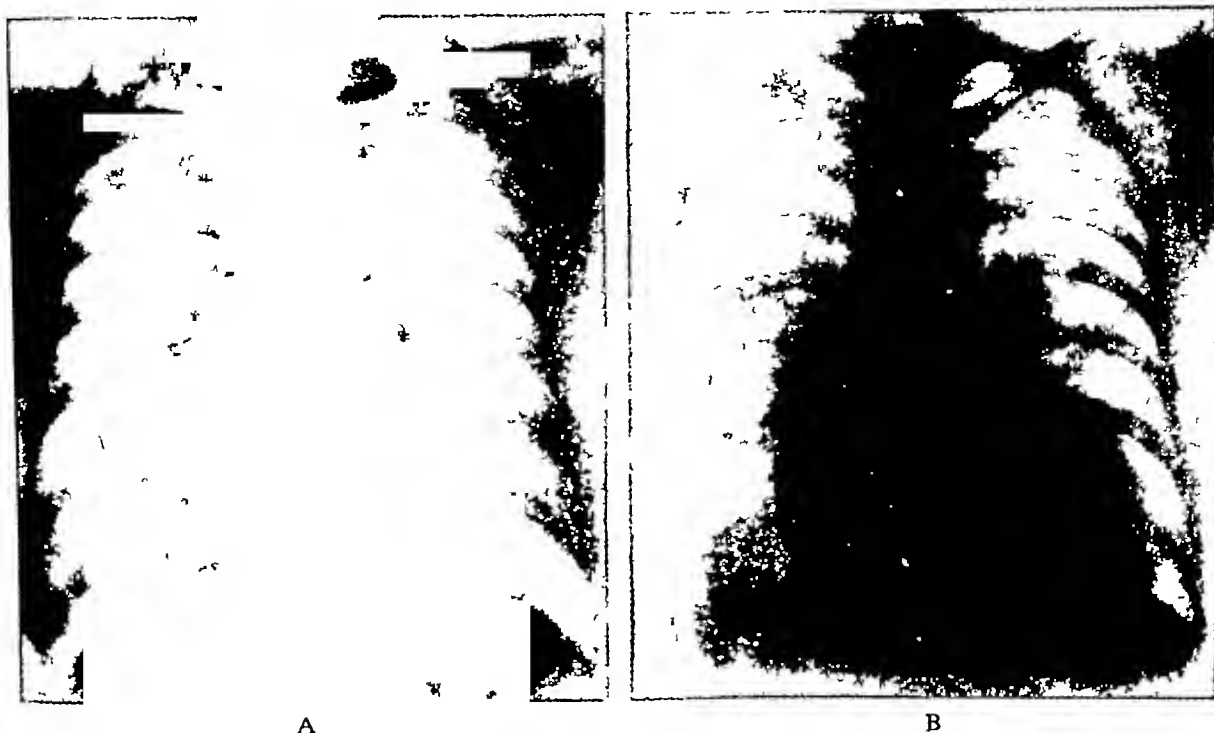
A B

FIG 4 —Teleradiograms showing cardiac enlargement in untreated subacute bacterial endocarditis   Case 8
(A) Six weeks before treatment   (B) Three days before treatment   A considerable change has occurred
in a few weeks

two cases it is difficult to account for the enlargement of the right ventricle and the changes
in axis deviation except by the development of increased mitral stenosis

These three cases suggest the possibility that stenotic valvular lesions may occasionally
develop or increase after successful treatment with penicillin, this is not unlikely since repair
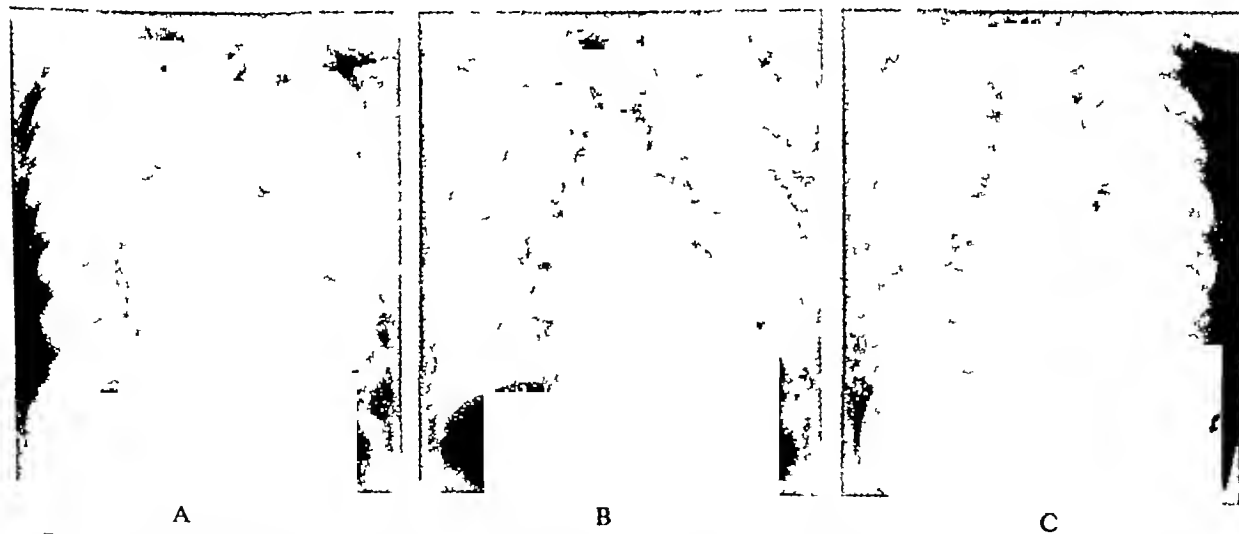
A B C

FIG 5 —Teleradiograms   Case 10   (A) Before treatment   (B) Twelve months after treatment
(C) Seventeen months after treatment, showing slight prominence of pulmonary conus
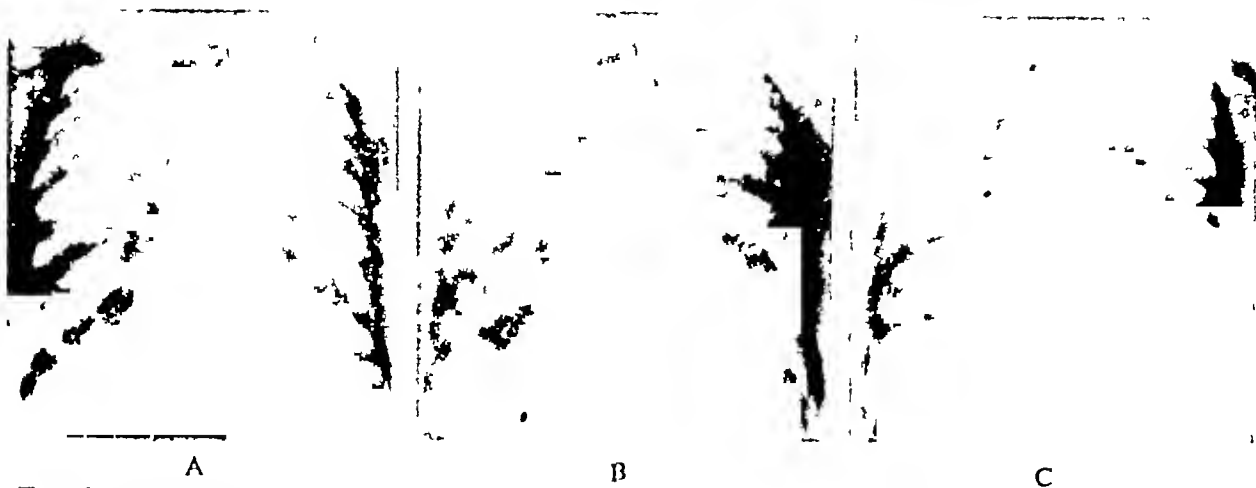
E

FIG 6—Teleradiograms showing progressive cardiac enlargement after control of infection   Case 22
(A) Before treatment   (B) Two months after treatment   (C) Nine months after treatment, showing
gross enlargement   (See cardiograms, Fig 7)
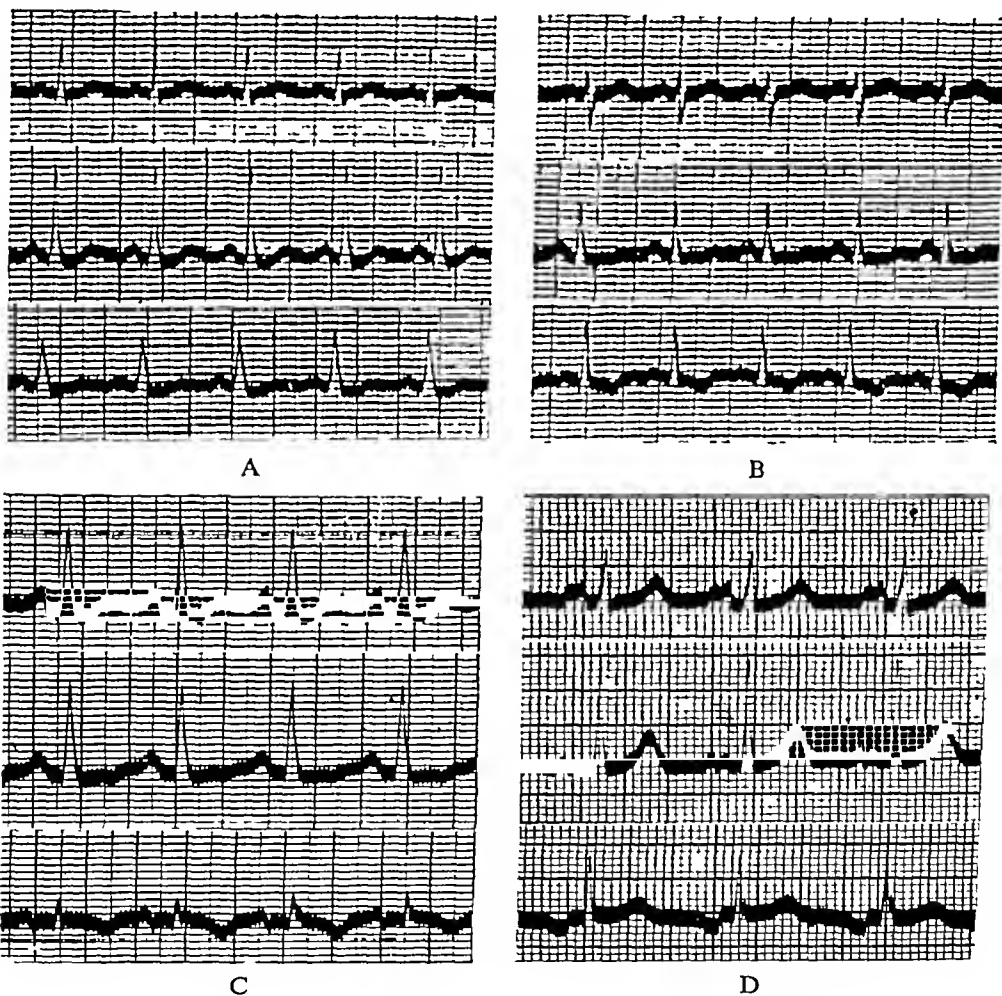
FIG 7—Cardiograms   (A) Case 22, during treatment   (B) Case 22, three months after treatment, showing
development of right axis deviation   (C) Case 17, during treatment   (D) Case 17, one year after
treatment, showing recovery of T waves, change in form of P waves and increase in voltage of QRS III
with decrease in voltage of QRS I, indicating a shift of the electrical axis towards the right   (Reduced
to four-fifths)

of the valvular damage is accompanied by fibrosis   If the infection largely destroys the valve, a stenotic lesion is most unlikely to develop during healing, it is the less damaged valve which will be liable to this complication   We cannot, of course, be sure that the changes are not due to the spontaneous progress of the rheumatic lesions but it is doubtful if this explanation is adequate
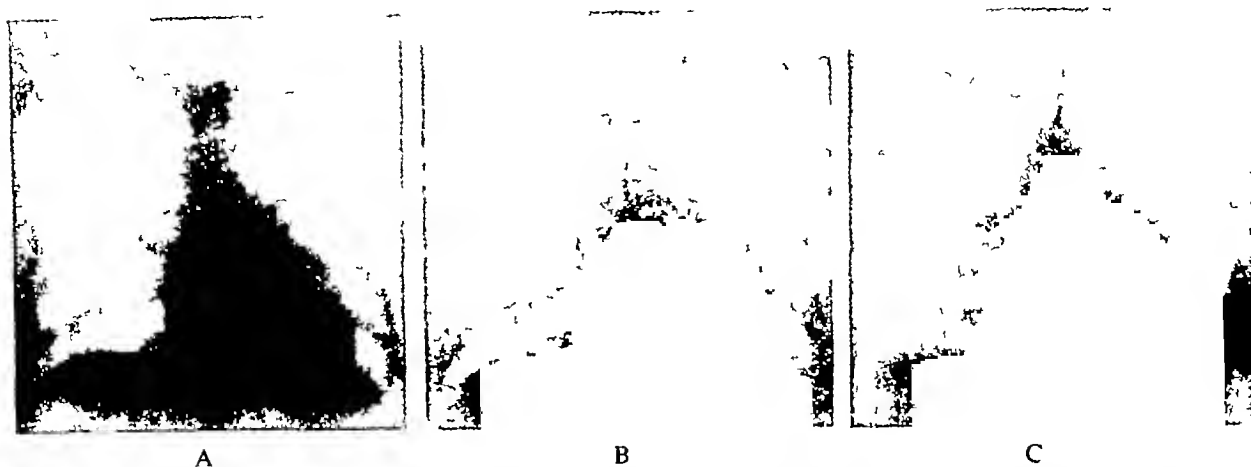
FIG 8 —Teleradiograms showing progressive cardiac enlargement after control of infection   Case 17
(A) Three days after treatment   (B) Four months after treatment   (C) Ten months after treatment
(See cardiograms, Fig 7)

Relapses

In 5 cases short courses of penicillin had been given before admission, a positive blood culture was subsequently obtained in all   In 3 the relapse occurred within two weeks and in the others at some unknown period within five weeks and four months respectively   It appears that when the relapse was promptly detected and adequate treatment instituted, recovery followed, but, in both cases in which there was delay in detecting the relapse the patient died

TABLE VII

RELAPSES FOLLOWING INITIAL COURSE AFTER ADMISSION

Case	Course	Time of relapse after end of course	Subsequent treatment	Result
1	1×5	0–5 days	$\frac{1}{2} \times 18$	Died
2	1×10	9–13 weeks	$\frac{1}{2} \times 28$	Well
3	$\frac{1}{2} \times 10$	21 days*	$\frac{1}{2} \times 28$	Well
4	$\frac{1}{2} \times 10$	0–9 days	$\frac{1}{2} \times 9$	Well
12†	$\frac{1}{2} \times 22$	0–6 days	$\frac{1}{2} \times 20$	Died

* No culture, recurrence of pyrexia
† Insensitive organism, died during second course

In 5 cases a relapse followed the initial course after admission (Table VII) in 3 cases within a week of the end of treatment, and in 1 case three weeks after treatment   The remaining case is interesting, thirteen weeks after a short course of treatment a positive culture was obtained although the patient was free from symptoms and there were no clinical signs of infection   Regular blood cultures are, therefore, necessary during convalescence for early detection of relapses which may not, at first, show much clinical deterioration   Two patients

whose infection relapsed following inadequate treatment after admission ultimately died, one was infected with an insensitive organism and the other, our first case, never had a full course of penicillin

Relapses following inadequate treatment, if promptly detected and adequately re-treated, do not appear to have prejudiced the ultimate outcome in these cases   In their case Florey and Florey (1944) found a four-fold increase in the resistance of the organism after treatment, they attributed this to penicillin therapy   Bloomfield and Halpern (1945) also found one case in which an organism, sensitive before treatment, became insensitive after treatment, and Christie (1946) considers that, in assessing the danger of inadequate treatment, this possibility ought not to be ignored   In one of our cases, in which the blood culture remained positive during treatment, the resistance of the organism increased from 4 to 18 times that of the Oxford staphylococcus   On the other hand, Meads et al (1945), Anderson and Keefer (1945), and Dawson and Hunter (1946) were unable to find any change in the resistance of the causative organisms in their cases   Since the measurement of resistance is open to criticism, the response to re-treatment may be a more reliable test, there is at present no evidence to suggest that if patients infected with an initially sensitive organism relapse after inadequate therapy, they will often fail to respond to a subsequent full course   Relapse after prolonged treatment may carry a graver prognosis as Christie (1946) has suggested   No patient in this series relapsed after a 28-day course but, from our subsequent experience, we know this can happen even if the organism is sensitive

UNSUCCESSFUL CASES

It is essential to know how often death is due to failure to control the infection   We have studied this problem in three ways   (1) by clinical assessment of the control of infection, (2) by histological assessment of the degree of healing, and (3) by post-mortem culture of the vegetations

Clinical Criteria of Control of Infection   In successful cases the blood culture became negative and the temperature fell to normal by the end of the first week   Recurrence of pyrexia in the second week was not regarded as significant if the blood culture remained sterile   Usually there was little rise in haemoglobin or gain in weight during treatment   After successful penicillin treatment the weekly blood culture remained sterile and the temperature was normal unless another infection was present or major infarction took place, the haemoglobin and weight increased steadily

Histological Criteria of Healing   In untreated subacute bacterial endocarditis the vegetation consists essentially of a thrombus lying on a valve and covered, wholly or in part, by a layer of organisms   Organization is present, for fibroblasts and capillaries grow into the thrombus from the valve and are associated with large mononuclear cells   Polymorphs, and frequently lymphocytes, indicate active inflammation at the base of the vegetation and in the adjacent valve

After penicillin therapy the first sign of healing was the disappearance of the active inflammatory lesion, removal of the hyaline thrombus by mononuclear cells then began and foreign-body giant cells appeared in the zone of bacteria   Although organisms were still present at this stage, they stained less readily and were presumably dead since cultures from the vegetation remained sterile   Finally, in the most advanced stage of healing that was seen, the thrombus was very small, often consisting of a little hyaline material lying on scanty fibrous tissue but sometimes calcified, when rather more fibrous tissue was found

The degree of healing was assessed solely on histological grounds, without reference to clinical evidence of control of infection or period of survival after the completion of treatment. The vegetations were classified, according to the degree of healing, into three stages. (Table VIII)

TABLE VIII

HISTOLOGICAL CRITERIA OF HEALING

Stage 1 —Indistinguishable from vegetations of untreated case—active inflammation
Stage 2 —Much organization, no inflammatory reaction (or only slight) intermediate between Stages 1 and 3
Stage 3 —Organization advanced, probably nearly healed

Feature	Stage 1	Stage 2	Stage 3
Polymorphs in vegetation or valve	Moderate number	Few or none	None
Mononuclear cells in vegetation	Some	Some	Few or none
Growth of endothelial cells over vegetation	Never	Never	Often
Newly formed fibrous tissue	Little	Much (cellular)	Variable amount
Organisms	Yes	Yes	Sometimes
Positive culture from vegetation	Sometimes	Never	Never

In untreated bacterial endocarditis, although acute inflammatory changes are always present in some part of the lesion, there may also be areas of healing, in assessing healing in these cases it was, therefore, necessary to examine several sections from each vegetation and to form an opinion from the composite picture   A general impression of the process of healing after penicillin therapy can be gained from the naked-eye appearances and these are illustrated in Fig 9

Post-mortem Culture of Vegetations   Before removal of the heart all the great vessels were tied, the heart was then removed intact   With aseptic precautions the ventricular wall

TABLE IX

CONTROL OF INFECTION AND DEGREE OF HEALING IN 15 FATAL CASES

Case	Time of death	Duration of normal temperature before death	Duration of sterile blood culture before death	Anatomical condition of vegetations *	Post-mortem culture of vegetations	Control of infection	Degree of healing
	During treatment						
5	6th day	2 days	—	—	—	?	—
20	6th day	3 days	2 days	Stage 1	Strept viridans	0	0
9	15th day	nil	nil	(a) Stage 1, (b) Stage 2	—	0	∓
12	20th day†	7 days	5 days	Stage 1	Sterile	?	0
25	20th day	5 days‡	14 days	Stage 1	Sterile	+	0
23	27th day	nil	nil	(a) and (b) Stage 1	B coli only§	0	0
30	27th day	24 days	24 days	(a) and (b) Stage 1	Sterile	+	0
	After treatment						
28	4 days	10 days‡	26 days	(a) and (b) Stage 2	Sterile	+	+
8	4 weeks	7 weeks	8 weeks	—	—	+	−
29	4 weeks	nil	8 weeks	Stage 2	Sterile	+	+
1	6 weeks	nil¶	8 weeks	(a) Stage 2, (b) Stage 3	Sterile	+	++
14	10 weeks	13 weeks	13 weeks	Stage 2	Sterile	+	+
26	10 weeks	10 weeks‡	13 weeks	—	—	+	−
6	13 weeks	16 weeks	17 weeks	Stage 2, (a) and (b)	—	+	++
7	13 weeks	16 weeks	17 weeks	(a) and (b) Stage 3	—	+	+++

* When more than one valve was affected the degree of healing is stated in both
† Two courses of treatment
‡ Penicillin pyrexia
§ B coli septicæmia during life
‖ B coli urinary infection
¶ Multiple pulmonary emboli after treatment

was incised, portions of the vegetations removed, ground up in a sterile mortar, and inoculated on to blood agar plates and into Hartley broth

The observations made in these three ways in 15 fatal cases are summarized in Table IX In Cases 5 and 20 death occurred too soon after beginning treatment to estimate the full effect of penicillin but the temperature had been rapidly controlled in both   In Case 20 however,
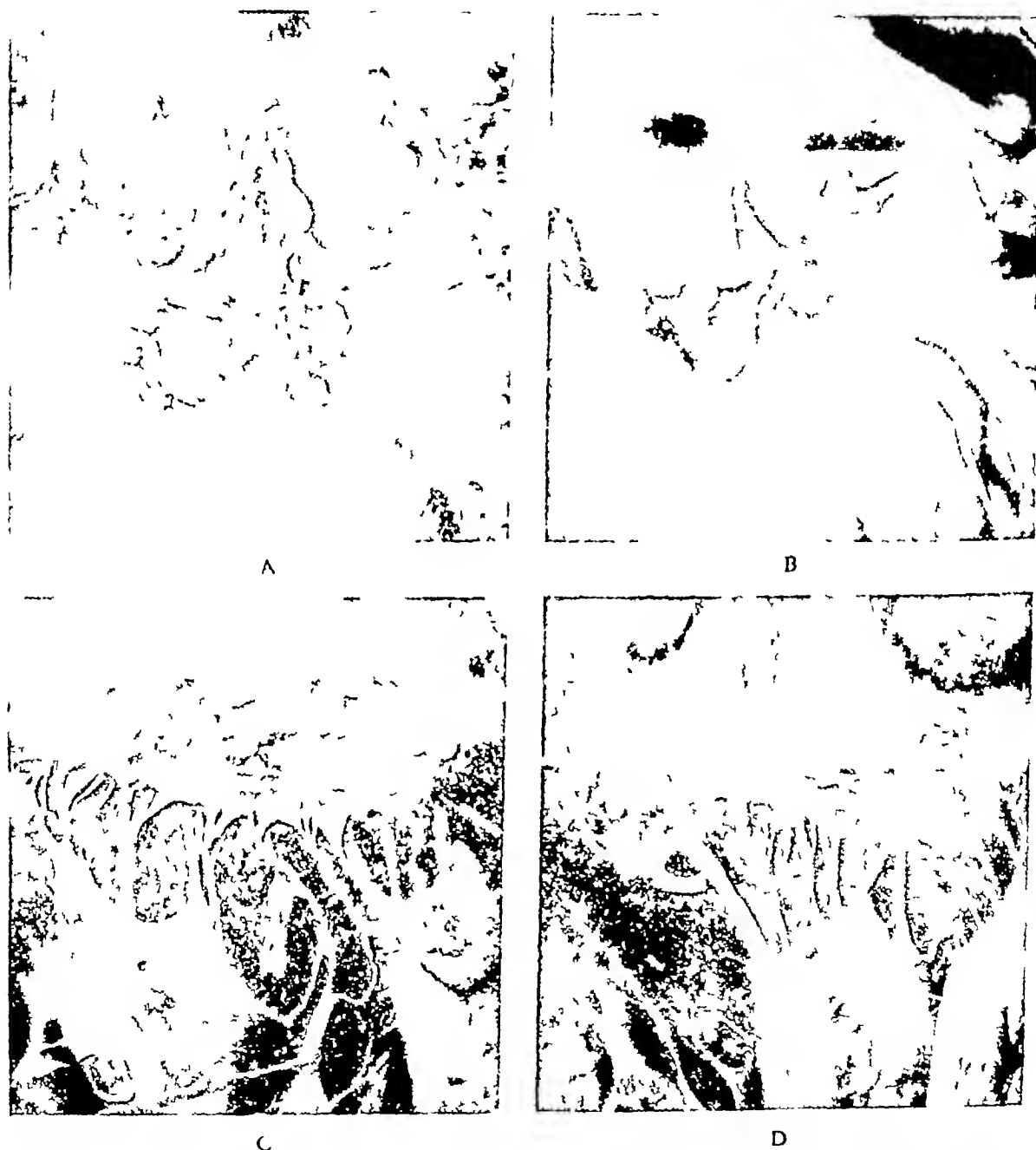
FIG 9 —Healing of vegetations after treatment   (A) Case 9 aortic valve   Death on fifteenth day of treatment, histologically indistinguishable from untreated case (Stage 1)   (B) Case 28, aortic valve   Death four days after treatment   vegetations histologically healing (Stage 2)   (C) Case 9, mitral valve Vegetations histologically healing (Stage 2)   Compare with unhealed lesion on aortic valve of same case (A)   (D) Case 7, mitral valve   Death thirteen weeks after completion of treatment   Vegetations almost completely healed histologically (Stage 3)

in spite of the sterile blood culture during life, *Strept viridans* was isolated from the vegetations after death   This type of case, in which a sterile blood culture can be obtained although living organisms are present in the vegetations, has been previously described by Meads *et al* (1945), it probably represents an early stage in the response to penicillin and may explain the need to continue treatment long after the blood is sterile

In Cases 9, 12, and 23, we cannot regard the infection as controlled, but there was some response to treatment in Case 12, this supports the suggestion recently made by Gordon and Zinnemann (1945) that some strains of *Hæmophilus influenzæ* are sensitive *in vitro* to high concentrations of penicillin   In the other two dying during treatment (Cases 25 and 30) the infection appeared clinically controlled and the vegetations were sterile at necropsy, but there was no histological evidence of healing

Eight cases died after treatment, in all the infection had been clinically controlled and cultures of the vegetations, made in four, were sterile   Evidence of healing was present in all the six examined histologically, and was more advanced in those who lived longest after treatment

Thus, of 13 cases dying after the first week of treatment, there is evidence of failure to control the infection in only 3, one of these showed some response clinically, and none completed a full course before death   Histological evidence of healing was not present until some time after clinical control of infection and sterilization of the valves, and did not reach an advanced stage until the infection had been clinically controlled for three months

Causes of Death

Since in most of our cases death cannot be attributed directly to the infection, other adequate causes of death should be demonstrable and this proved to be so   heart failure, uræmia, or vascular accidents were the usual immediate causes (Fig 10)   In Table X the clinical causes of death are compared with the post-mortem findings in 13 cases   Infection was a direct cause of death only when the patient died during treatment and major embolic
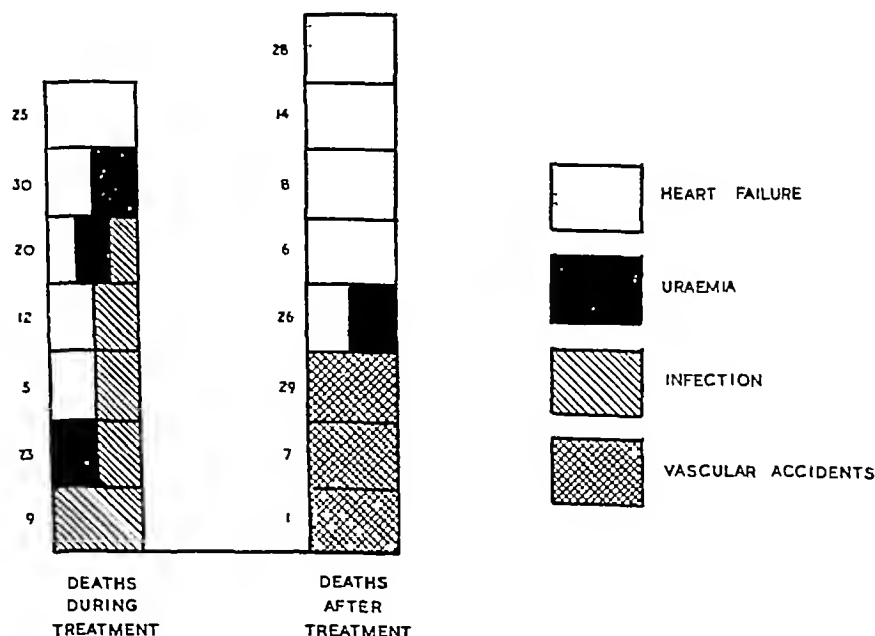
FIG 10 —Diagram showing clinical causes of death in 15 cases   When more than one factor appeared important, all have been represented

accidents led to death only in those surviving treatment   Heart failure and uræmia occurred in both groups

Heart failure was the most important cause of death for of 18 cases without failure only 2 died, whereas of 15 with failure 13 died, in 5 of these heart failure was the sole cause of death, in 5 it was a major factor, but in 3 failure was not severe when death occurred from other causes

TABLE X

CAUSES OF DEATH

Case	Time of death	Clinical cause of death	Principal post-mortem findings
	During treatment		
5	6th day	1 Left heart failure 2 ? Infection	1 Pulmonary œdema 2 Active myocarditis 3 Hypertrophy and dilatation of left ventricle 4 Nephritis
20	6th day	1 Uræmia 2 Right heart failure 3 ? Infection	1 Nephritis 2 Congestive (systemic) heart failure
9	15th day	Infection	1 Pulmonary œdema (slight) 2 Active myocarditis 3 Hypertrophy and dilatation of left ventricle
12	20th day	1 Acute left heart failure 2 ? Infection	1 Pulmonary œdema (much) and congestion 2 Nephritis
25	20th day	Left heart failure leading to right	Congestive (systemic) heart failure
23	27th day	1 Uræmia 2 Infection	Pyelonephritis
30	27th day	1 Uræmia 2 Right heart failure	1 Nephritis 2 Congestive (systemic) heart failure 3 Bronchopneumonia
	After treatment		
28	4 days	Acute left heart failure	1 Pulmonary œdema (moderate) and congestion 2 Active myocarditis 3 Hypertrophy and dilatation of left ventricle
8	4 weeks	Left heart failure leading to right	No necropsy
29	4 weeks	Cerebral hæmorrhage	Cerebral hæmorrhage
1	6 weeks	Pulmonary infarction	Pulmonary infarction
14	10 weeks	Left heart failure leading to right	1 Congestive (systemic) heart failure 2 Pulmonary œdema (slight) and congestion 3 Peritonitis
26	10 weeks	1 Uræmia 2 Left heart failure leading to right 3 Acute hepatitis	No necropsy
6	13 weeks	Left heart failure leading to right	1 Congestive (systemic) heart failure 2 Bronchopneumonia
7	13 weeks	1 Cerebral hæmorrhage 2 Pulmonary embolism from femoral venous thrombosis	1 Cerebral hæmorrhage 2 Pulmonary embolism and femoral venous thrombosis

Heart failure usually developed when considerable cardiac enlargement was present (Table XI) and it is interesting to consider the factors upon which the size of the heart depended The size before infection is naturally a factor but, unfortunately, we generally have no record of this   As we have shown, the progress of the infection leads to a progressive increase in the heart size in all those where we have data bearing on the point   It is, therefore, to be expected that the longer the infection has been present the larger the heart will be, on comparing the heart size before treatment with the duration of the illness (Table XI) it was found that of 7 patients with cardiothoracic ratios of 1 5 or less, 6 had suffered from symptoms of infection for fifteen or more weeks and 6 had heart failure, whereas of 8 without cardiac enlargement, only 1 had been ill for more than fifteen weeks   This direct relation between the dura-

tion of the bacterial endocarditis and the heart size suggests that cardiac damage owing to the infection plays an important part in producing cardiac enlargement and heart failure

Myocardial lesions and valvular damage may both be important in the production of cardiac enlargement and heart failure in untreated bacterial endocarditis   The inflammatory and embolic myocardial lesions have been studied in the untreated disease by Bracht and Wachter (1909), Saphir (1935), and De Navasquez (1939)   Small coronary emboli, structurally similar to the vegetations, appear to be common histologically, De Navasquez (1939) demonstrated such lesions in 16 of his 20 untreated cases   The lesions studied by Bracht and Wachter (1909) led to destruction of muscle tissue and some healing took place in the untreated disease

TABLE XI

COMPARISON OF HEART SIZE, INCIDENCE OF HEART FAILURE, DEATH, AND DURATION OF INFECTION

Cardiothoracic ratios	Number of cases	Number with heart failure	Number of deaths from heart failure	Number with symptoms of infection for 15 or more weeks
2 0 or more	8	1	0	1
1 9 or 1 8	7	1	1	2
1 7 or 1 6	6	4	2	3
1 5 or less	7	6	6	6
Totals	28*	12	9	12

* Five cases, unfit for cardioscopy, omitted

The histology of the myocardium has been examined in 13 of our cases, our examination was not exhaustive for routine sections were taken only from a standard site in the ventricular septum though sometimes additional sections from other parts of the myocardium were examined   Fibrotic and inflammatory lesions were present in 9, these were severe in 5 cases Libman and Friedberg (1942) were inclined to minimize the importance of myocardial lesions, but heart failure was a principal cause of death in 4 or our 5 cases with severe lesions whereas this was true of only half of those with slight lesions or no lesion   Although these figures are not incompatible with the contention of Buchbinder and Saphir (1939) that myocardial lesions play an important part in the production of heart failure, there can be little doubt that valvular damage is often more important as Bloomfield *et al* (1945), Bloomfield and Halpern (1945), and Rosenblatt and Loewe (1945) found in their cases   In our Case 25 the blood pressure suddenly altered from 140/90 to 145/55 owing to rupture of an aortic cusp three days before treatment, this led to heart failure and a change in the cardiothoracic ratio from 1 8 to 1 4   Death occurred 23 days later and the valve perforation was confirmed at necropsy Since the infection frequently attacks the aortic valve, failure will often be associated with aortic incompetence, as Mokotoff *et al* (1946) showed   Of our 29 cases with rheumatic heart disease, 16 had aortic incompetence on admission and 10 of these developed failure, 2 others developed aortic incompetence under our observation and failure followed in both, whereas heart failure occurred in only 2 of 11 without aortic incompetence   If damage to the aortic valve by the infection is an important cause of failure, we should expect left heart failure to be common   Excluding one case in which failure was associated with a congenital lesion, left heart failure was present in 10 of our cases and was followed by right heart failure in 6, 9 of these had aortic incompetence   In 3 right heart failure was present on admission, all 3 had aortic incompetence and we cannot be certain that left heart failure had not been

present in the earlier stages, but there was no history of paroxysmal dyspnœa   In the remaining case right heart failure developed during treatment

In short, heart failure was present in nearly half and was a principal cause of death in two-thirds of those that were fatal   Recovery was uncommon in those with failure and the rule in those without it   Heart failure occurred principally after long-standing infection and was generally associated with much cardiac enlargement and aortic incompetence, it was usually left-sided at the onset   Both myocardial and valvular damage due to the infection were probably factors in producing failure but the valvular lesions played the more important part   As most of our patients had only slight cardiac lesions before the infection, we consider that the cardiac damage due to the infection played a more important part than the underlying congenital or rheumatic lesion in causing failure   Since the infection usually attacks the aortic valve, the frequency of left heart failure and its association with aortic incompetence support this contention

Renal Damage   Impairment of renal function was found clinically in 10 cases, in one other no renal function tests were made before death on the sixth day of treatment but at necropsy a severe nephritis was present   Renal impairment never appeared for the first time during or after treatment   As Levy and McKrill (1946) found, the longer the duration of infection the greater the proportion of patients with severe renal damage (Table XII)

TABLE XII

COMPARISON OF DURATION OF SYMPTOMS WITH RENAL IMPAIRMENT AND WITH NUMBER OF DEATHS

Duration of symptoms of infection	Number of cases	Number with impaired renal function	Number of deaths
Less than 10 weeks	7	1	0
10–19 weeks	13	4	4
20–29 weeks	7	3	5
30 or more weeks	6	3	6

Of these 11 patients with severe renal damage only 2 recovered, in one case the standard urea clearance was 19 per cent on admission and the blood urea 104 mg per 100 c c , during the third week of treatment the figures were 68 per cent and 48 mg per 100 c c and two weeks after treatment the urea clearance was 96 per cent and the blood urea 34 mg per 100 c c   In the other case the initial urea clearance was 40 per cent and the blood urea 42 mg per 100 c c , during treatment the blood urea rose to 64 mg but eight weeks after treatment it was 26 mg and the urea clearance 86 per cent   Renal function also improved in 2 of the 9 fatal cases, in 4 no serial data are available, and in 3 the renal impairment increased before death   Four died in uræmia with final blood urea levels of 484, 220, 152, and 148 mg per 100 c c , additional possible causes of death were present in all (Fig 10)

It was possible to study the renal histology in 11 of 15 fatal cases, the clinical and histological findings are summarized in Table XIII   In 4 of these 11 there was severe, and in 2 slight impairment of renal function before death, but none had hypertension during life   All the 4 with severe impairment of renal function had a severe nephritis histologically, as did one without renal function tests during life   In 4 cases this was a diffuse glomerular nephritis, 2 acute and 2 subacute, and in 1 pyelonephritis was found   In the 2 with slight impairment of renal function the only lesion was glomerular fibrosis not unlike that described by Bell (1932) in untreated subacute bacterial endocarditis, this was also present in 5 others and 2 of these were known to have no clinical impairment of renal function   In 2 there was increased intercapillary hyaline material similar to that found by Ellis (1942) in his Type II nephritis, neither had nitrogen retention during life   The typical focal glomerular necroses of embolic

nephritis were present in only 2 cases and these changes were limited to a few glomeruli   The renal histology thus showed a variety of changes and was characterized by the frequency of diffuse glomerular lesions, whereas focal embolic lesions were uncommon

TABLE XIII

KIDNEYS—CLINICAL AND HISTOLOGICAL FINDINGS   (11 CASES)

Case number	5	6	7	9	12	20	23	25	28	29	30
Blood pressure	120/30	115/85	150/80	120/50	125/25	110/75	150/50	140/90	150/50	105/60	130(/0)
Urea clearance	—	83%	—	60%	30–75%	—	17%	89%	60%	—	60% –
Blood urea	—	24	—	26	66–22	484	124–148	26	28	36	56–220
Gross abnormality urinary deposit	+			+	+	+	+	—	—	+	+
B coli urinary infection	+	—	—	—	—	—	±	—	—	+	—
Acute diffuse glomerular nephritis	+										±
Subacute diffuse glomerular nephritis					+	+					
Pyelonephritis							+				
Glomerular fibrosis	+	+	+	+				+	+	+	
Increased intercapillary hyaline material		+								+	
Focal glomerular necrosis	±									+	

Libman and Friedberg (1942) described diffuse glomerular nephritis in untreated bacterial endocarditis and found it more frequently in the bacteria-free stage   They considered that it led to progressive renal impairment and death from uræmia in at least one-third of their cases dying in the bacteria-free stage and remarked on the absence of hypertension, unless present before the nephritis   Loewe and Rosenblatt (1945) recorded one case, unsuccessfully treated with penicillin, with diffuse glomerular nephritis but no focal glomerular lesions, the blood pressure was 120/80, and later 120/40

Thus diffuse glomerular lesions, without hypertension, occur not infrequently in bacterial endocarditis   The presence of gross renal insufficiency in 2 of our recovering cases, and the improvement of renal function in 2 of our unsuccessful cases, suggests that similar types of renal damage may be compatible with recovery after penicillin therapy   If this is so, it is possible that when renal function is impaired during the active stage, progressive renal insufficiency may develop long after successful treatment, a long-term study of recovering cases with past renal impairment should decide this

Major Embolic Accidents   There were 21 patients with major embolic accidents, 17 before treatment, 8 during treatment, and 4 after treatment, the sites of lodgement were pulmonary in 6, cerebral in 7, renal in 8, splenic in 7, retinal in 3, and coronary in 1 case   The smaller number of major emboli during treatment is of little significance since the period of treatment was short compared with the duration of infection before treatment, but it is clear that major emboli are rare after treatment, if we exclude the 3 with cerebral or subarachnoid hæmorrhage in which embolization may have occurred some time previously, major emboli occurred after treatment in only one, who were never fully treated (Case 1)

One of the cases with cerebral hæmorrhage is interesting   Following a cerebral embolus nine months before treatment, she developed a left-sided hemiparesis which almost completely recovered, three months after the end of treatment, while apparently well, she suddenly collapsed unconscious with a severe left hemiplegia, she died five days later   At necropsy, a cerebral hæmorrhage had largely destroyed the right lenticular nucleus and internal capsule   It seems likely that the cerebral embolus led either to a mycotic aneurysm or to an area of softening but, owing to the disorganization of the affected area at necropsy, we were unable to determine which of these had caused the hæmorrhage   Cerebral embolism, with apparent recovery, may thus lead to fatal cerebral hæmorrhage many months after the infection is controlled

Major emboli may occur at any stage of the disease, 3 of the 31 major emboli marked the onset of symptoms of infection, 11 occurred in the first ten weeks of the illness, 9 in the second ten weeks, and 8 subsequently

SPECIAL TYPES OF CASE

Associated with Pregnancy   In 7 of our 22 female cases the infection began during pregnancy (Table XIV), this is a remarkably large number for Page and Campbell (1939) were able to find records of only 15 cases of subacute bacterial endocarditis associated with pregnancy when they published their own 3 cases   In the first two diagnosis was delayed one of these was moribund on admission and died six days later, in the other the infection was controlled but death occurred three months after treatment from cerebral hæmorrhage The other five were treated early and did well in spite of major vascular accidents in two and heart failure in one   Six children are well but in one case a macerated fœtus was expelled a few days before the beginning of treatment

TABLE XIV

CASES ASSOCIATED WITH PREGNANCY

Case	Age	Stage of pregnancy at onset	Time before treatment	Confinement	Child	Mother	Remarks
5	26	Term	28 weeks	Normal	Well	Died	Regarded as puerperal pyrexia
7	23	Term	46 weeks	Normal	Well	Died	Regarded as puerperal pyrexia
3	19	33 weeks	10 weeks	Normal	Well	Well	Coronary embolism during treatment
10	22	20 weeks	6 weeks	Cæsarean section	Well	Well	Subarachnoid hæmorrhage at 34th week
18	28	20 weeks	5 weeks	Forceps for 2nd stage delay	Well	Well	Blood culture negative 24th week, positive 25th week
27	23	32 weeks	11 weeks	Normal	Well	Well	Dental extraction 23rd week pregnancy
31	29	23 weeks	5 weeks	Abortion 28 weeks	Macerated	Well	Admitted for heart failure, pyrexia, culture positive

Thus, provided the infection is promptly detected and adequately treated, the prognosis is good for mother and child   As these patients are usually under supervision, owing to the association of heart disease with pregnancy, the opportunity for early diagnosis is not lacking Since confinement may have to be undertaken during the difficult period of convalescence, when the heart is unfit to carry additional burdens, it may be advisable to eliminate the physical strain of labour by Cæsarean section, particularly if there is likely to be any obstetrical difficulty

With Patency of the Ductus Arteriosus   One of our patients, a girl of 13, had a patent ductus arteriosus infected by a pneumococcus   She had suffered from lassitude and pyrexia for three months before admission, and was then emaciated, very toxæmic, and severely dyspnœic owing to multiple pulmonary infarcts   The infection was controlled by a 28-day course of penicillin and her general condition improved, but she developed a left pneumothorax (Fig 11), possibly from rupture of a septic subpleural infarct   Her subsequent progress was satisfactory and four months after treatment the ductus was ligated by Mr Graham Bryce   Penicillin cover was used and there were no post-operative complications   After operation the heart decreased in size (Fig 11)

Ligation of the infected ductus has given surprisingly good results (Shapiro and Keys, 1943, Tubbs, 1944, Gilchrist, 1945) but the success of penicillin in controlling the infection makes it possible to treat the infection first and, when the condition of the patient has improved, to ligate the ductus   Vesell and Kross (1946) have reported a successful case in which the ductus was ligated six days before the end of a 30-day course of treatment   They suggest

immediate operation if the organism is insensitive or the duration of infection more than three months or the response to penicillin doubtful   We do not yet know how often penicillin will control infection in a patent ductus but the general condition of our patient on admission excluded chest surgery and the ultimate result justified the attempt to control the infection by penicillin before contemplating surgical ligation of the ductus   If the infection of the ductus can be arrested by penicillin, this will lead to such improvement that the risk of subsequent surgical intervention will be materially diminished   We, therefore, consider that this method of management should receive adequate trial

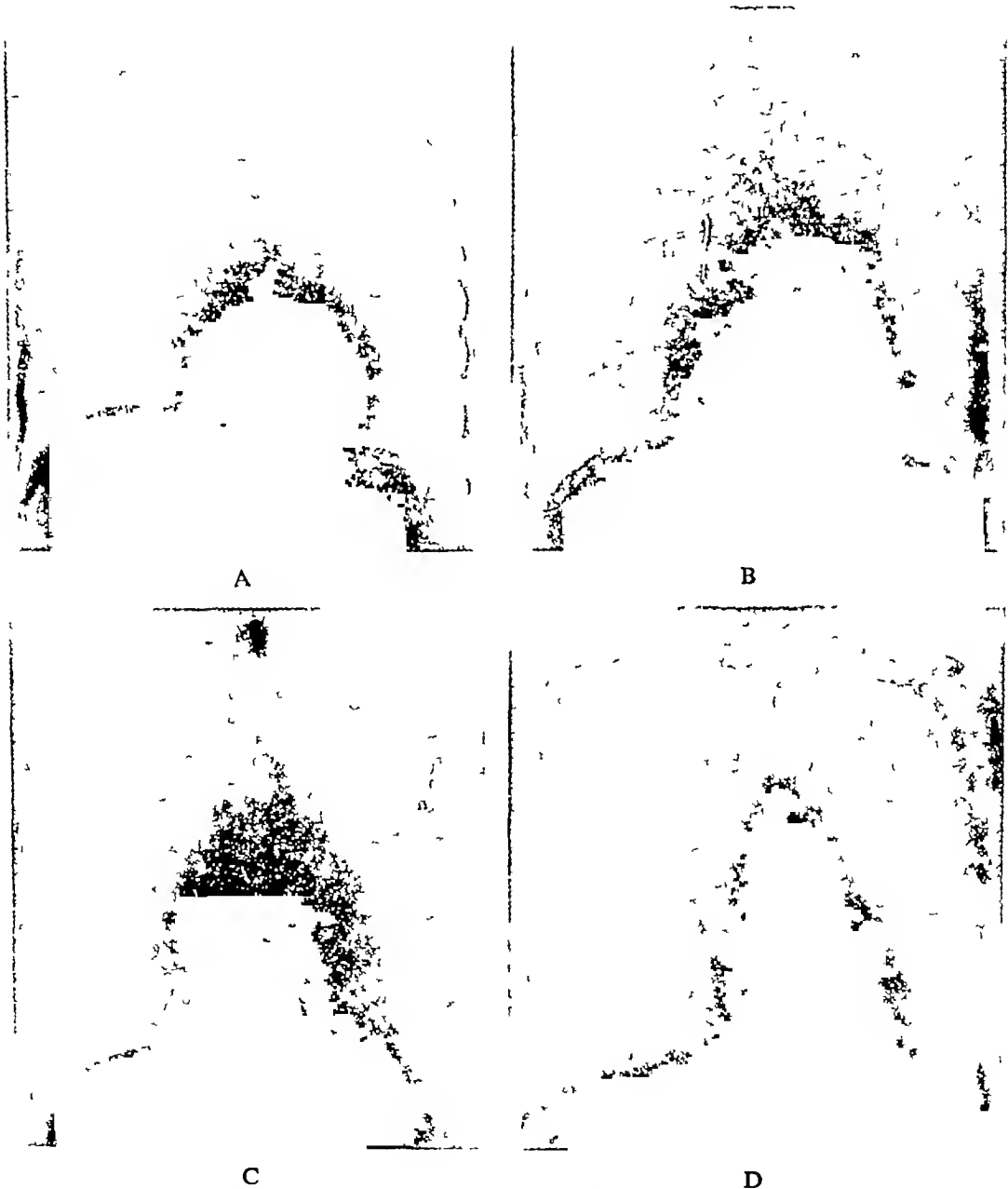Fig 11 —Infected patent ductus Teleradiograms   Case 33 (A) Two months before treatment (B) Fourth week of treatment, showing left pneumothorax and cardiac enlargement   (C) Three months after treatment and one month before ligation of ductus, showing absorption of pneumothorax but persistence of cardiac enlargement   (D) Two months after ligation of patent ductus, showing decrease of heart size

PROGNOSIS

Although failure to control the infection has rarely been a hindrance to success, yet nearly half our patients died With such a means of arresting the disease in our hands we cannot be satisfied with this mortality and must seek to reduce it Although we have studied only a small series, much evidence has been presented to indicate that the longer the duration of the infection the larger the heart, the more frequent renal impairment, and the more often do heart failure and uræmia prevent recovery It is, therefore, to be expected that the mortality will be principally determined by the duration of infection, this has been illustrated in Table XII When symptoms had been present before treatment for less than 10 weeks no patient died, none with symptoms for 30 or more weeks recovered and only two with symptoms for 20 or more weeks

When we come to consider other factors it is more difficult to draw conclusions It seems reasonable to suppose that the severity of cardiac damage before infection will play a part in leading to death when the additional burden of infection is added but, if we judge the severity of the underlying cardiac lesion from the patients' capacity for exertion before infection, no clear correlation with mortality emerges—6 of 17 cases in Class I died, 8 of 13 in Class II, and 1 of 3 in Class III Unfortunately the last group with much reduced capacity for effort is too small to be useful, and the mortality may not be significantly higher in the intermediate group than in the apparently fit Since the underlying heart disease was comparatively slight in most cases, it may be unimportant compared with the severe damage that may occur when the infection remains untreated for months

In this series all patients over 50 years of age died, but there was no relation between age and mortality in the younger age groups On comparing the number of deaths in each group with the duration of symptoms of infection it became clear that the mortality was determined by the duration of symptoms and not by the age This is confirmed by the fact that two patients over 50 years of age, treated subsequent to this series, have both made good recoveries

Factors such as the heart size (see Table XI) and the hæmoglobin level before treatment can be attributed to the infective process When the hæmoglobin was over 70 per cent 2 of 9 cases died, when it was between 50–69, 9 of 16 cases died, and when it was under 50, 4 of 8 cases died The degree of correlation between heart size on the hæmoglobin level and the mortality may be merely another indication of the severity and duration of infection

TABLE XV

COMPARISON OF RESISTANCE AND NUMBER OF ORGANISMS WITH NUMBER OF DEATHS

Resistance*	Number of cases	Number of deaths	Number of organisms per c c blood	Number of cases	Number of deaths
Less than 1	9	4	Less than 25	6	4
1–5	20	9	25–100	9	1
Over 5	3	2	101–1000	9	5

* The resistance of the organism is expressed as a multiple of the resistance of the Oxford staphylococcus

Provided the causative organism is sensitive to penicillin, neither the estimated degree of resistance to penicillin nor the number of organisms per c c of blood appear to be related to the mortality (Table XV) The importance of the resistance of the organism may be masked by the inaccuracy of the method of measurement, or the resistance may be truly unimportant up to a point, since the level of penicillin in the blood probably allows a safe margin unless the organism is insensitive

With a much larger series it may prove justifiable to attach greater importance to some of these factors, but in our cases we are convinced of the importance of only one   the duration of the infection before treatment   This is, fortunately, a factor we can influence by early diagnosis and prompt treatment, if this can be achieved the present mortality should be materially reduced

Failure of the patient to seek medical advice in the early stages is a most serious obstacle to the early diagnosis of some diseases, but this does not appear to be so in subacute bacterial endocarditis, for nearly three-quarters of our patients (24) were either under regular supervision for their heart disease at the onset of symptoms of infection, or sought medical advice when the first symptoms appeared   Of the other 9 only 4 delayed more than four weeks before seeking advice   The mortality is, therefore, closely related to the period under medical observation   If the disease had been suspected when these patients first sought advice, repeated blood culture by an adequate technique would have established the diagnosis, for, even with infections of short duration, we had no difficulty in isolating the organism   In these early cases non-specific symptoms predominate and signs are few, if penicillin treatment is to be successful the diagnosis must be suspected before the classical physical signs appear, for they indicate that the disease is well advanced and should serve as a warning that arrest of the infection may not avert death from heart failure or uræmia

SUMMARY

The treatment of subacute bacterial endocarditis by penicillin is described in 33 unselected cases with 15 deaths, the minimum period of observation after the completion of treatment was six months

The clinical features of these cases, the methods of investigation, and the technique of laboratory procedures are described _

The clinical response to adequate treatment is described and the importance of careful management during convalescence is emphasized

The degree of recovery is assessed in 18 successful cases, although most patients resume their old occupations, increased residual cardiac damage is the rule and a small proportion may develop stenotic valvular lesions during healing

Relapses following inadequate therapy, if promptly detected and adequately treated, do not appear to prejudice the ultimate outcome

The clinical and pathological evidence indicating control of the infection in unsuccessful cases is assessed, it is concluded that the infection was controlled in all cases completing treatment.

The process of healing is studied histologically in 12 cases   healing is not advanced until three months after clinical control of the infection

The causes of death in 15 cases are discussed with a description of the post-mortem findings in 13 cases   The importance of heart failure in causing death is emphasized   Cardiac damage by the infection is the important cause of failure

The renal lesions are studied histologically in 11 cases   diffuse, not focal, glomerular lesions predominate, and it is concluded that, if similar lesions occur in successful cases, they may lead to future renal insufficiency

Seven cases associated with pregnancy are recorded, 5 mothers and 6 children survived

In one case with an infected patent ductus arteriosus the ductus was ligated four months after successful penicillin treatment

The factors that may have played a part in the outcome of treatment are discussed, evidence

INFECTIVE ENDOCARDITIS OF THE TRICUSPID VALVE
REPORT OF A CASE DUE TO STREPTOCOCCUS VIRIDANS

BY

I M LIBRACH

From the City Isolation Hospital, Nottingham
Received September 9 1946

Post-mortem evidence shows that tricuspid lesions are more common than is generally supposed, though they often escape clinical recognition   Gilchrist and Lyon (1933) found that 10 per cent of 109 cases with mitral stenosis had tricuspid stenosis, and Coombs (1924) found that about one-third of all cases of rheumatic endocarditis had tricuspid involvement That this lesion should pass undiagnosed during life is not surprising, for the physical signs are less constant

Endocarditis lenta *per se* is unfortunately a common enough condition, but it affects in the main the left side of the heart   Though a fair number of cases of tricuspid endocarditis due to various organisms, such as gonococcus and pneumococcus, have been reported, comparatively few were due to *Strept viridans*   Boldero and Bedford (1924), though they stress the frequency of infective endocarditis and congenital abnormalities, do not mention one case of tricuspid endocarditis in a series of 602 that they collected from various authors, and also confirm the relative infrequency of infective endocarditis of the right heart, mentioning only 30 cases affecting the pulmonary valves, that is 5 per cent   Hentel (1942) mentions one case, Marques *et al* (1941) another, a patient with congenital tricuspid stenosis and auricular fibrillation, who developed infective endocarditis as a terminal event, and Hacker (1931) a third with a ruptured spleen and a subcapsular hæmatoma   Melnick *et al* (1935) and Oerting (1931) also cite cases—the latter in a male, aged 46, where no blood culture had been done, but the diagnosis was confirmed post-mortem   Horder (1908) in a series of 118 post-mortem examinations, in a total number of 150 cases, mentions 14 with tricuspid involvement, together with mitral and aortic infection or both   no case of tricuspid disease occurred alone and the infection was generally pneumococcal

CASE RECORD

A male, aged 50 years, married and a shopkeeper by trade, consulted his doctor three weeks before admission to hospital, with a history of constant cough for seven days, which confined him to bed   On examination then, he had signs of pneumonia, temperature 102, respiration 36, pulse 120, but very few physical signs   He complained of pain in the right shoulder and chest midway in front   On exhibition of sulphapyridine, the temperature fell to normal in seven days, the pulse remained at 100, but rose two days later in spite of further sulphathiazole The temperature continued to rise to 103° F , the urine contained albumin, and as the temperature would not settle, he was advised to go into hospital   His previous history and family history were not pertinent

On admission, 8/4/43, he was seen to be a thin frail man of pale colour, temperature 100, pulse 98, respiration 24   The tongue was a fiery red with some furring   The teeth were very foul   There were no signs in any system, except some impaired resonance over the right basal region with diminished breath sounds and crepitations   The blood pressure was 138/90 and a white blood count was 8850 with 55 per cent neutrophils and 32 per cent

F

ymphocytes   A radiogram of the chest showed doubtful unresolved pneumonia in the right upper zone

He was put on sulphamethazine, 4 g to start with and 2 g every six hours   Two days later his temperature had fallen and he felt slightly better   The sulphamethazine was stopped after a total of 26 g had been given   On 12/4/43, his temperature began to swing upwards again   The chest showed crepitations in both mid-zones, without localizing signs, but it was thought that a lung abscess might be present   On 14/4/43, the total white cells rose to 11,050 of which 89 per cent were neutrophils   Another radiogram of the chest showed doubtful tuberculosis in the right mid-zone, but the sputum contained no acid-fast bacilli   A course of sulphadiazine was started on the 16th, but soon given up as there was no response   There were still no localizing signs but pallor and a polymorphonuclear leucocytosis persisted, no spleen was felt, but a blood culture and Widal were done and both were negative to abortus and the coli-typhoid group   On the 21st the right lung was explored but no pus was found and blood from the lung was sterile on culture

On the 25th, he was transfused with one pint of blood, and on the 26th with a further pint, he was started again on sulphathiazole, to a total of 32 g, and this seemed to bring the temperature down   Petechiae appeared on the trunk, and on the 30th, systolic and diastolic murmurs were audible at the lower end of the sternum   An infective endocarditis was considered and blood culture which was repeated now grew a pure growth of *Strept viridans*   On May 4th, a systolic murmur appeared at the aortic area   On the 7th, the systolic bruit at the base of the sternum was much louder, and suggested tricuspid endocarditis   On the 9th the patient became semi-comatose and died

Post-mortem examination (Dr Johns)   Generalized petechial rash over body and limbs

Chest   Right lung, adherent, left, free   Some congestion with early hypostatic pneumonia

Heart   Gross pericarditis with early pus formation in the pericardial sac   A large mass of rough soft friable vegetations on the posterior cusp of the aortic valve   A smaller, harder, not so friable mass situated on a cusp of the tricuspid valve   No other abnormality of mitral or pulmonary valves   Heart muscle soft and friable   Coronary arteries patent   No gross atheroma   No emboli or thrombosis in great vessels   No sign of chronic rheumatism

Abdomen   Solid organ congestion   Intestine showed petechial haemorrhages   No emboli or aneurysm seen

Brain   Some pus in basal cisterns, which on staining showed streptococci in fair numbers.

Diagnosis.   Subacute bacterial endocarditis with pericarditis and terminal meningitis

DISCUSSION

This case is interesting from several aspects   The left heart is more frequently injured in endocarditis lenta, except in pneumococcal cases when according to Preble (1904), the relative frequency of right-sided involvement is greater than in acute endocarditis in general   Both sides were involved in this case   Allen (1935) suggests that in cases affecting the right heart, it is due to the fact that the more virulent the organism, the less necessary the violence of the impact necessary to secure its lodgement   He points out that patients with auricular fibrillation rarely develop endocarditis, because blood drools through the valve concerned

Boldero and Bedford (1924) think that the access of arterial blood to the right heart in congenital cases with patent septa may explain the unusual frequency of dextral endocarditis in this type of case, but in our case both sides were affected, though there was no septal defect   A possible explanation of this is that put forward by Hadfield and Garrod (1942)   they postulate that when the pressure of any chamber is raised above the normal, this predisposes to trauma of the related valves and to endocarditis, so that when for example mitral incompetence is present, thus raising the pressure in the pulmonary circuit, right sided involvement is a

frequent finding Von Glahn and Pappenheimer (1935) claim that the disease attacks valves, the seat of recent, not old, rheumatic infection, as is usually thought In this case there was no evidence of any rheumatic infection of a valve, nor was there any rheumatic history, recent or remote Another well-known important point, is that the *Strept viridans* will attack valves that are congenitally malformed, such as bicuspid aortic valves In this case there were no signs of congenital abnormality

What is the source of infection in this disease? Horder (1908) showed that infective endocarditis was pre-eminently a streptococcal disease (for streptococci occurred in 66 per cent of his series of 40 cases) and that the types most often found on blood culture were those present in fæces and normal saliva, i e *S fæcalis* and *S salivarius* He also pointed out the absence of any visible focus of infection and later showed that pressure on an apical root abscess forced the contents of the abscess into the lymphatics (quoted by Hadfield and Garrod, 1942) This work has been confirmed by Okell and Elliott (1935), who performed a series of blood cultures on patients undergoing dental extraction, and found bacteræmia in 75 per cent of those examined In their analysis they agree with Horder that the vast majority of streptococci in infective endocarditis are of the salivary or *S viridans* type, a fact which has been amply confirmed since These abound in the mouth and its neighbourhood, especially in the condition of oral sepsis In 110 cases of pyorrhœa, 12 were found in their series to have a streptococcal bacteræmia at the time of examination, irrespective of operative procedure, i e in persons with severely septic mouths, streptococci usually of the viridans type may enter the blood-stream in the absence of any obvious trauma This leak is obviously not a blood infection and will depend on the rapidity of the phagocytic clearance of the blood-stream, and though of little account in the normal person, may determine an endocarditis in those with diseased or malformed valves In our case, the man had a mouth full of foul teeth, but unfortunately no culture was made of the organisms therein The amount of septic absorption taking place must have been on a considerable scale and probably *S viridans* was present in the gums

Pus formation is usually not a feature of this disease It occurred in two places, the pericardium and cerebral meninges both showing *S viridans* on direct examination—in this case, probably as a terminal event owing to the intense final bacteræmia and pyæmia

At the time of treating this case, penicillin was not available, and it, therefore, illustrates the uselessness of sulphonamide therapy alone

A note on the diagnosis of a tricuspid lesion *per se*, might not be out of place The characteristic features described are the intense venous engorgement with systolic pulsation of the deep and superficial veins, *especially the jugular*, due to the large rise in the systolic pressure in the right auricle, and the presystolic and systolic murmurs with reduplication of the second sound at the xiphisternum Van Bogaert and Mortelmans (1942) emphasize the importance of the *persistence* of these signs in any case, while Bramwell and King (1942) stress the fact that the P wave of the cardiogram is of unusually high voltage Finally, in cases with combined mitral and tricuspid lesions, Röslers' sign is valuable, namely, radiography of the heart showing a lack of dilatation of the left auricle due to the tricuspid lesion decongesting the pulmonary circuit, and so relieving the burden of the auricle

SUMMARY

A case of endocarditis lenta affecting the aortic and tricuspid valves, in a man of 50 years, is described

The dangers of oral sepsis in cases with known heart disease are stressed

In the diagnosis of the individual lesion, the significance of the persistence of systolic and presystolic bruits at the xiphisternum is emphasized

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ABSTRACTS OF CARDIOLOGY

The Construction of the Cardiac Vector R F HILL
Amer Heart J, **32**, 72–81, July, 1946

This article should be helpful to workers new to the field of cardiac vector study The frontal plane cardiac vector may be constructed by measurements of potential differences in leads I, II, and III, or by obtaining the potential values at the right arm, left arm, and left leg by means of Wilson's unipolar lead. In the first method, directions are obtained from the sides of Einthoven's triangle or from their representation in Bayley's triaxial system, in the second method they are derived from axes joining the centre of Einthoven's triangle to its apices If the scalar measurements in method I are called e_1, e_2, and e_3 respectively, and those in method II are called V_R, V_L, and V_F, then we have the equations $e_2 = e_1 + e_3$, and $e_2 = V_F - V_R$, but the author points out that this last relationship is invalid when the measurements are turned into vectors, and shows that under these circumstances $V_L - V_R = e_1\sqrt{3}$, $V_F - V_R = e_2\sqrt{3}$, and $V_F - V_L = e_2\sqrt{3}$ Incidentally it is emphasized that the equation $e_2 = e_1 + e_3$ has nothing whatever to do with Einthoven's triangle, but holds good for the relationship between any three points in an electrical field when considered as a closed loop, and when the galvanometric connections are arranged as they are in electrocardiography *Paul Wood*

The Effect of Theophylline Aminoisobutanol on the Circulation in Congestive Heart Failure F U STEINBERG and J JENSEN *J Lab clin Med*, **31**, 857–865, Aug, 1946

The effect on the circulation of theophylline aminoisobutanol (0 24–0 48 g intravenously) and (in a smaller number of cases) of aminophylline and sublingual glyceryl trinitrate was studied The venous pressure was followed for 1 or 2 hours and the circulation time measured frequently, generally with " decholin " In nearly all of 14 cases tested there were falls in venous pressure and reductions in the circulation time Considerable variations in the venous pressure were noted There was generally an immediate rise after venepuncture and after coughing, vomiting, or straining Relaxation or sleep caused a fall The injection of theophylline usually caused an abrupt fall, sometimes this reached its lowest almost at once, always within half an hour In the cases where the dose was 0 48 g the fall varied between 8 and 77 with an average of 37 mm of water Aminophylline (0 48 g intravenously) and nitroglycerin (0 6 mg sublingually) were equally effective, but the fall seemed to be a little more lasting with

aminophylline In a few patients there was no fall with any of these drugs and the results were rather inconstant from day to day The fall was not accompanied by any change of plasma volume The average circulation time was shortened by 10 seconds the duration of the effect was not measured carefully but it seemed to be about an hour

The authors conclude that theophylline has a useful place in the treatment of congestive failure, but mainly in emergencies because the effect begins to wear off quickly *Maurice Campbell*

Observations on the Effect of Theophylline Aminoisobutanol in Experimental Heart Failure J R SMITH and J JENSEN *J Lab clin Med*, **31**, 850–856, Aug, 1946

Following the demonstration of Steinberg and Jensen that in patients with congestive heart failure theophylline aminoisobutanol lowered the venous pressure and shortened the circulation time, the authors have used the heart–lung preparation of the dog to investigate this action further Heart failure was produced by adding 0 20 per cent chloral hydrate to the perfusing fluid (generally 0 8 g in all) The subsequent addition of theophylline aminoisobutanol (0 06 g) to the perfusing blood generally stimulated the myocardial contractions with restoration of function, so that pulmonary œdema and congestion were removed promptly (usually within 1 minute) Dilatation of the heart was overcome and the cardiac output increased The strength of the cardiac beats was increased, and this did not seem to depend on any increased coronary arterial flow It is concluded that the clinical benefit previously observed was due to improved myocardial function and pulmonary flow and that peripheral vasodilatation might also help in producing the improvement *Maurice Campbell*

Fluids in Congestive Heart Failure. C M LEEVY, J A STRAZZA, and A E JAFFIN *J Amer med Ass*, **131**, 1120–1125, Aug, 1946

Some clinicians are now departing from the practice of restricting fluid intake in congestive heart failure, this communication advocates giving the patient as much fluid as he desires, or even forcing fluids It is believed that restriction of intake to 2 pints (1 1 litre) daily or less may lead to dehydration of the tissues and toxic effects such as pyrexia and mental changes A high fluid intake is held to facilitate the excretion of waste products by the congested kidney

The authors report the results of an investigation of 122 patients with congestive failure to determine

the relative advantages of restricted fluids, fluids *ad libitum*, and forced fluids All received a special diet containing little salt, while other routine methods of treatment for congestive failure were the same in the 3 groups Mercurial diuretics were used " only when the degree of œdema was a major source of discomfort " Of those on restricted fluid (not more than 1200 ml daily) and those on forced fluids (up to 7600 ml daily) about equal proportions (one-sixth of the total) were unable to adhere to the regime because of the ensuing discomfort Failure symptoms disappeared in the same time, after about 10 days, in each of the 3 groups Of 36 patients in the restricted fluid group 1 developed symptoms attributed to dehydration When fluids were forced no adverse effects were noted on dyspnœa, heart rate, circulation time, venous pressure, or cerebral function The regime of fluids *ad libitum* was best tolerated [These results suggest that fluid limitation in congestive failure is less necessary than has been assumed, and that it may on occasion be harmful, but they do not show dehydration toxaemia to be other than an exceptional result The special diet used would be difficult to arrange in home treatment]

Harold Cookson

Circulatory Failure. [In English] J McMichael *Schweiz med Wschr* , 76, 851–857, Sept , 1946

The " back-pressure " theory of cardiac failure, based on the idea that the veins are passive tubes, becomes obsolete with the knowledge that alterations in venous tone and calibre affect cardiac output Starling showed from heart-lung preparations that the venous inflow directly governed the output of the heart, as the filling pressure rose the output increased, but when a certain point of distension was reached further stretching of the heart lowered its output In early failure the heart's output is not significantly reduced, though its capacity for improvement is diminished Output drops later in failure Accurate estimations of output and filling pressure by Cournand's method of right auricular catheterization, performed without mishap in over 500 cases since 1941, have shown that in valvular and hypertensive heart disease with failure the rise in venous pressure is not the back-pressure effect of a falling output but a compensatory mechanism to maintain an optimal output The first rise in venous pressure occurs when the output is only slightly below normal As failure advances the venous pressure rises and output falls to 3 litres per minute (normal 5 3)

Digitalis is found to reduce the venous pressure, this is followed in the normal heart by a fall in output and in the failing heart by a rise Similar results are obtained by venesection, irrespective of the ventricular rate, which suggests that the value of digitalis lies primarily in its action on venous pressure rather than in its slowing effect on heart rate in auricular fibrillation That digitalis takes a venous overload off the heart is supported radiologically by evidence of reduction in heart size, and clinically by the equally

good results of digitalization in failure with normal rhythm Anæmia, emphysema, thyrotoxicosis, beriberi, traumatic arteriovenous aneurysm, and Paget's disease are characterized by high cardiac output In severe anæmia blood volume is always reduced, indicating that the venous congestion is due to compensatory increase in venous tone and reduction of vascular bed In anæmia with hæmoglobin below 30% the output is doubled, venous pressure high, and pulse fast These patients are already in a critical condition with venous congestion and œdema, and transfusion may be dangerous by further increasing venous pressure, unless given slowly with digitalis Digitalis alone, by reducing venous pressure, upsets this compensatory equilibrium and is, therefore, dangerous in heart failure from anæmia, emphysema, and acute or chronic cor pulmonale For similar reasons it is useless in shock In Paget's disease, where the effect of the increased skeletal circulation resembles arteriovenous aneurysm, failure occurs with high output and raised venous pressure In pericardial tamponade the rise in venous pressure is again compensatory to maintain an effective cardiac filling pressure

Peripheral circulatory failure (shock) is no longer believed to be due to pooling of blood in the veins or to hæmoconcentration With hæmorrhage the effective volume of circulating blood is reduced and the heart's filling pressure and output cut down, but peripheral resistance is raised The lowered blood pressure is due more to lack of vasoconstriction than to reduced cardiac output, which seldom falls below 3 litres per minute Later vaso-vagal fainting may occur (with slow pulse and fall in blood pressure) from sudden vasodilatation of arterioles in skeletal muscles Overwhelming bacterial toxæmia reduces both venous pressure and cardiac output, though suprarenal cortical damage may contribute Further work on non-surgical shock suggests that peripheral vasodilatation and high cardiac output exist in early diabetic acidosis

[The direct clinical application of some of the methods discussed in this paper have to be confirmed In the failing heart the importance of the coronary circulation and of the balancing mechanism between right- and left-sided stress are additional factors of importance that call for consideration]

J L Lovibond

Experiences with Dicumarol in the Treatment of Coronary Thrombosis with Myocardial Infarction. I S Wright *Amer Heart J* , 32, 20–31, July, 1946

Dicoumarol was used in cases of coronary thrombosis The indications for its exhibition were (1) repeated minor attacks of thrombosis, (2) embolic phenomena indicating intracardiac thrombosis The procedure was as follows The prothrombin time was estimated (13 to 14 seconds is normal) If normal or lower, 300 mg of dicoumarol was given by mouth Each morning the prothrombin time was

determined again, and afterwards a further dose of 300 mg was given until the time was 30 seconds, or 100–200 mg if between 30 and 35 seconds When over 35 seconds the drug was discontinued until the time had fallen to 30 seconds Smaller doses were then resumed (100 mg) The course lasted 30 days Hæmorrhagic manifestations occurred with the prothrombin time at 60 seconds, and were relieved by 300–500 ml of fresh blood, and by vitamin K (menadione bisulphite) 64 mg in 1 to 4 doses

The results seemed to show a diminished mortality in the 76 cases observed There was no unfavourable effect on the heart *Terence East*

Testosterone in Angina Pectoris. E B LEVINE and A L SELLERS *Amer J med Sci*, **212**, 7–11 July, 1946

Twenty-four male patients, average age 56 years, were treated with androgens The authors conclude from this series that androgens are ineffective in the treatment of angina, though they consider that their results show that testosterone, especially in the form of testosterone propionate by injection, is of definite value in relieving the chest discomfort of the climacteric or of cases of neuro-circulatory asthenia in men of the angina age group *P M F Bishop*

Congenital Aortic Atresia. N H ISAACSON, S D SPATT, and D M GRAYZEL *J Pediat*, **29**, 222–225, Aug , 1946

Pheochromocytoma and Chronic Hypertension. D M GREEN *J Amer med Ass*, **131**, 1260–1265, Aug , 1946

A case of pheochromocytoma is reported and 50 additional records from the literature are discussed. In cases where the paroxysmal features are overshadowed there is a remarkable resemblance to idiopathic hypertension After the removal of an encapsulated renal tumour all the symptoms improved In an analysis of 50 cases from the literature it is found that the majority are chronically hypertensive, and only a minority manifested intermittent hypertension Of this latter group surgical removal of the tumour interrupted the disease in 12 of 14 patients It is suggested that all patients with functioning pheochromocytoma will progress to a stage of chronic hypertension if they live long enough, and evidence of cardiovascular and renal disease then becomes common In the interval between paroxysms in the intermittent type, kidney dysfunction is recorded in only 4 of 14 cases In 22 cases in which the symptoms had progressed to a state of chronic hypertension, and with a mean duration of 4 years, there was a uniform fall in blood pressure after operation, and a retrogression of cardiovascular-renal abnormality *G Hesketh*

Temporal Arteritis D A DANTES *J Amer med Ass*, **131**, 1265–1269, Aug , 1946

The author reports a case of temporal arteritis, and discusses 27 unquestionable cases recorded The youngest was 55 years of age, the average age being 65 years Pain is prominent, commonly in the temporal region A temperature persists for several months, and there may be malaise and sweats Ocular disturbance is common, œdema, exudates, retinal hæmorrhages, and thrombosis of the retinal artery all occurring Symptoms suggesting cerebral involvement have been observed Characteristically a segment of one or both temporal arteries is prominent, indurated, nodular, and tender, and pulsation may be lost Adjacent arteries may be affected Complete clinical recovery occurs in the majority of cases, but permanent visual impairment may result from the retinal lesions *G Hesketh*

Potential Variations of the Right Auricular and Ventricular Cavities in Man H H HECHT *Amer Heart J*, **32**, 39–51, July, 1946

Intracardiac catheterization has made it possible to record, by means of an electrode in the right side of the heart, the changes in electrical potential in the venæ cavæ, right auricle, and right ventricle in the human subject It has been supposed that the unipolar lead (VR) from the right arm recorded the potential variations within the cavities of the heart In this investigation 5 cases were studied. Two had right bundle-branch block, 1 had left bundle-branch block, and 2 had left ventricular enlargement. The position of the electrode was located by fluoroscopy

There were three interesting observations (1) At high auricular levels there are large predominantly negative auricular deflections Endocardial auricular deflections are always biphasic and show a QRS type of deflection and are often followed by a T wave At the lower levels a positive wave, which is called PR (like R in QRS), appears (2) Ventricular complexes from the junctional area show negative deflections in a normally activated heart, and in left bundle-branch block The deflections are positive in right bundle-branch block (3) Ventricular complexes recorded at the higher auricular levels are different from those recorded at the lower levels and from the cavity of the right ventricle They resemble those of the unipolar lead on the right arm (VR) In the auricle there is an area of primary and persistent electro-negativity which presumably corresponded to the site of the pacemaker away from which impulses spread, hence the negative sign Records from the right ventricular cavity in left bundle-branch block do not differ from those in normals, for the left-side lesion does not affect the polarization of the right side When there is right bundle-branch block the right ventricular endocardial curve is positive This is due to the fact that the septum and right ventricular cavity are activated from the left side and so a layer of positive charges faces the right ventricular cavity

These observations are in accord with the new nomenclature of bundle-branch block, and agree with the assumption that the action currents in the heart muscle are to be regarded as an electrical " source " (positive) followed by an electrical " sink " (negative

The ventricular deflections from the higher auricular level differ from those of the right ventricular cavity because they represent the combined changes in the two ventricles together. When activation is normal these are negative. Such are the deflections of the right arm unipolar lead. If there is left bundle-branch block the right ventricular negativity will predominate. In right bundle branch block the initial negative deflection is derived from the left ventricle but the broad positive deflection from the right ventricular cavity. [It would have been interesting to have had some normals.]   *Terence Fast*

The Influence of Drugs on the T Wave of the Electrocardiogram after Exercise (Über den Einfluss vegetativer Pharmaka auf den Ablauf der T-Zacken-Veränderungen im Arbeits Elektrokardiogramm) A WALSER *Cardiologia* 10, 231–250 1946

Slight exertion and severe exertion were found to influence the height of T in opposite senses. Severe exertion caused an initial increase of T followed by a prolonged decrease. Slight exertion caused an initial decrease of T followed by a prolonged increase. The previous injection of sympatol-atropine accentuated the initial and the late changes in the height of T after severe exertion. Previous injection of physostigmine-gynergen accentuated only the initial increase in T after severe exertion but caused a more rapid return to the previous level. Neither sympatolatropine nor physostigmine-gynergen caused a decisive difference in T-wave behaviour after slight exertion. The author concludes that parasympathetic excitation leads to an increase in the height of the T wave
      G Schoenewald

Heart Disease in Pregnancy W B STROMME and K KUDER *Amer J Obstet Gynec*, 52, 264–272, Aug, 1946

Stromme and Kuder review the previous publications on this subject from the department and then analyse a further 720 cases of heart disease in pregnancy. They show that maternal mortality from sepsis and hæmorrhage have so far decreased that in the series analysed heart disease was the leading cause of maternal mortality. Rheumatic disease was responsible for 91 per cent of the heart cases, congenital lesions accounted for 4 per cent and hypertensive disease for 2 per cent. The authors stress the importance of evidence of decompensation or fibrillation. This is claimed to be often a legitimate indication for termination of pregnancy and sterilization.

The importance is stressed of careful supervision of all cases and treatment of selected ones in hospital. Heart disease was detected in 3 per cent of all obstetric cases analysed. Therapeutic abortions were performed in 8 per cent, and for delivery forceps were used more and Caesarean sections less than in the previous series reported from the same department. The total mortality rate was 12 per 1000 cardiac cases and the mortality in the group admitted as

emergencies was 7 times that of the group which received antenatal care   *J Stallworthy*

The Clinical Use of Cytochrome C in Patients with Intermittent Claudication S PROGER and D J DEZANIS *Bull New Engl med Center*, 8, 145–147, Aug, 1946

The improved utilization of oxygen in the tissues resulting from the use of cytochrome C, on which the authors had previously reported (*J clin Invest*, 1945, 24, 864), led them to examine its effects in cases of intermittent claudication. Cytochrome C was given intravenously in doses of 50 mg daily to 13 patients suffering from intermittent claudication due to thrombo-angitis obliterans or arteriosclerosis. Of these, 3 showed no improvement, 3 definite but moderate improvement, and 7 striking improvement. This was assessed by means of exercise tolerance tests, involving stair climbing and level walking. Controls were made with the injection of an inert solution similar in colour to that of cytochrome. The characteristic response was increase of exercise tolerance which reached a maximum after 10 injections and was maintained for a long time after the injections had been discontinued, in 1 case almost a year   *B Samet*

The Effect of Meals on the Electrocardiogram in Normal Subjects E SIMONSON, H ALEXANDER, A HENSCHEL, and A KEYS *Amer Heart J*, 32, 202–214, Aug, 1946

The effect of meals on the electrocardiographic records in 12 normal adults was studied and the results were analysed statistically. An hour after moderate meals significant changes were observed—increase of heart rate, K_{QT} and QRS amplitude, decrease of T wave, duration of mechanical systole and QT interval, and left axis shift of the T axis. These changes were independent of the proportion of fat in the meal   *W J H Butterfield*

Changes in the Cardiovascular System in Scrub Typhus in Early Convalescence W LIKOFF *Amer J med Sci*, 211, 694–700, June, 1946

The authors have investigated 100 Service patients in the convalescent stage of scrub typhus. Symptoms relating to the cardiovascular system, including tachycardia at rest, dyspnœa, præcordial pain following exercise, and syncope, were present in 30 per cent of the cases, and in only 2 of these were average daily pulse rates of under 100 recorded.

In the asymptomatic group—70 cases—only 4 patients had daily pulse rates of over 100. No evidence of organic valvular disease or cardiac failure was noted in any of the cases. Ten patients—all in the symptomatic group—gave electrocardiographic abnormalities. Three showed persistent bundle-branch or intraventricular block. Transient changes recorded included delayed A-V conduction, negative T waves in two or more leads, and slurring of the QRS complex without prolonged duration
      A Henderson-Begg

The Incidence of Palpable Dorsalis Pedis and Posterior Tibial Pulsations in Soldiers J J SILVERMAN *Amer Heart J*, 32, 82–87, July, 1946

The average age of the 1014 soldiers studied by one observer was 20, and 90 per cent were under 22 Absence of pulsation in the dorsal artery of the foot and in the posterior tibial together on the same side occurred in 0 5 per cent, posterior tibial pulsation was absent on one side in 5 6 per cent, dorsalis pedis in 25 per cent Both posterior tibials were impalpable in 1 7 per cent, and both dorsal arteries of the foot in 7 5 per cent There was a significant difference between white and negro soldiers in these respects Among the white men one or other posterior tibial artery could not be felt in 2 per cent, and one or other dorsal artery of the foot in 27 1 per cent, whereas among the negroes these figures were 8 per cent and 6 6 per cent respectively

[No precautions against the effects of cold, emotion, or other factors are described] *Paul Wood*

Cor Pulmonale in Ankylostoma Infection E GARCÍA CARRILLO *Arch Inst Cardiol Méx*, 16, 154–158, May 31, 1946

Five cases in which the patients died from anæmia, ankylostomiasis, and multiple pulmonary emboli are presented with brief clinical and pathological findings Both peripheral phlebitis of infective origin and peripheral circulatory stasis give rise to repeated pulmonary emboli These factors combined with the poor nutritional state and anæmia of the majority of these patients are held sufficient to account for the heart failure and subsequent fatal issue

W T Cooke

Acute Pericarditis in Young Adults R M NAY and N H BOYER *Amer Heart J*, 32, 222–223, Aug, 1946

Forty-six cases of pericarditis occurring in soldiers, aged 18 to 37, were investigated by the authors at one of the American army rheumatic fever centres The diagnosis was based on clinical findings—præcordial or substernal pain, pain on breathing, swallowing, and twisting the trunk, pain worse when lying prone, the presence of friction rubs, radiological evidence of effusion, and electrocardiographic changes The patients could be divided into 3 groups (1) 25 patients in whom the pericarditis was associated with signs and symptoms of rheumatic fever, (2) 15 patients in whom the lesion was of undetermined aetiology, (3) 6 patients in whom it was associated with other diseases, such as aneurysm or pleural effusion

The leads studied were the standard limb leads and the apical lead, IVF Elevation of S–T segments, in most cases in more than 1 lead, occurred during the first 10 days after the onset of pericarditis in more than half of the patients seen early There was no reciprocal depression of S–T segments in leads that did not shows S–T elevation In 41 cases there was striking inversion of T waves and in more than half the cases the T waves were negative, diphasic, or iso-electric in all 4 of the leads These inversions were usually noted 5 days to 3 weeks after the onset of the disease and might persist for a few days or many weeks These changes are thought to be highly specific, but repeated electrocardiograms are necessary to detect them *E B G Reeve*

Foreign Bodies in and in Relation to the Thoracic Blood Vessels and Heart. III Indications for the Removal of Intracardiac Foreign Bodies and the Behaviour of the Heart During Manipulation D E HARKEN and P M ZOLL *Amer Heart J*, 32, 1–19, July, 1946

This article describes the removal of 26 pericardial and 13 intracardiac missiles The reasons for operation are held to be (1) prevention of embolism of the foreign body or associated thrombus, (2) reduction of danger of bacterial endocarditis, (3) prevention of recurrent pericardial effusion, (4) diminution of the incidence of myocardial damage It is most important to locate the foreign body accurately and plan the operation so that the maximum facility of exposure is obtained The heart tolerates dislocation badly The ventricles may dilate, and interference with the outflow of blood may lead to circulatory collapse Various arrhythmias, especially showers of extrasystoles, were noted Bundle-branch block may occur The surface of the heart must be kept moist Suturing and superficial manipulation were well tolerated Intracardiac manipulations were less well borne Location of fragments is difficult, and many thought to be in the heart were really outside it

Terence East

Ligation of the Ductus Arteriosus A R GILCHRIST *Edinb med J*, 53, 346–354, July, 1946

The persistence of a patent ductus arteriosus in extra-uterine life is known to carry with it certain severe complications in a proportion of cases Infection with *Streptococcus viridans* leading to infective endarteritis and septic emboli is a condition of the gravest severity, and a varying amount of disability may result from the interference with ordinary circulatory mechanics Both these complications can be overcome by occlusion of the ductus surgically

The mechanical effects of a patent ductus are due to the fact that the pulmonary artery has to receive blood from both the right ventricle and the higher-pressured aortic stream via the ductus The output of the left ventricle is thus stressed unduly to the extent by which it loses blood through the ductus This effect can be observed under the radiological screen, when the forcible contraction of the left ventricle and excessive pulsation of the pulmonary artery may be obvious The pulmonary artery may also be prominent and the vascular fields of the lung increased Clinically the characteristic murmur is usually present, but it may not attain its continuous quality for some years Below the age of 5 the signs are more equivocal and other signs, as mentioned

above, should be sought for There is, in addition, the increased pulse pressure, which may be very noticeable after exercise The fall in diastolic pressure following exertion is quickly restored, but when it can be recognized is a valuable diagnostic sign Infection in the pulmonary artery develops at an area opposite the ductus entrance Vegetations form and as they fragment are carried into the lungs as emboli Radiologically, patchy opacities appear in the lung fields, and a positive blood culture is often obtained Prolonged sepsis leads to cardiac enlargement with congestive failure

Three cases of well-established infective endarteritis were submitted to operation, there were 2 fatalities from massive pulmonary collapse and 1 dramatic recovery The author insists that " surgical ligation in the infected case is the only treatment to consider," and early diagnosis is of the greatest importance Every case of known patent ductus with an unexplained pyrexia should be suspect

In non-infected cases the reasons for surgery should be considered under several headings (1) restoration of normal circulation and improvement of development, (2) prevention of infection, (3) prevention of later circulatory incapacity and congestive failure A series of 36 cases in this class was studied, and 16 were operated on In the surgical ligation series there were 2 deaths, 1 following a repeat operation (the ductus having re-canalized after original occlusion with catgut ligatures) Of the remainder there was 1 instance of apparent re-canalization and 2 of partial, ductus closure, all other cases show very satisfactory results

The choice of age for operation, in the absence of infection or cardiac symptoms, lies between 7 and 10 years Over the age of 20, operation should be reserved for cases that show definite symptoms or signs of disability The operation is one which requires the specialized team-work of thoracic surgery Complications in the form of haemorrhage, pulmonary collapse, pleural effusion or infection may occur, but in the hands of experienced surgeons are rare

T Holmes Sellors

Acute Rheumatism J A Glover *Ann rheum Dis*, 5, 126–130, June, 1946

The incidence of acute rheumatism among trained troops has always been below expectation, in spite of the rigours to which they have been exposed But it does occur in the form of " barrack epidemics " among recruits crowded into training centres The author tabulates the estimated incidence of rheumatic fever among troops engaged in the Crimean, American Civil, South African, and Great Wars, and shows that there has been a steady decline in incidence and severity of the disease He writes " This astounding fact—that in the wet, the mud, and the stench of the trenches in Flanders in 1915 acute rheumatism was much less prevalent than in the high and magnificent climate of South Africa—seem to show that the disease had already begun its long decline in incidence and severity " Such a decline has been found in civilian as well as in military medicine In 1937 the death rate from rheumatic fever was less than a quarter of that in the period 1891–1900 It is claimed that the period between the two world wars was noteworthy in the history of rheumatic fever, for the decline in incidence of the disease, for the inception of systematic effort to prevent its ravages, and for the support for the theory that it is due wholly or in part to infection by the *Streptococcus pyogenes*

The theory of streptococcal responsibility for rheumatic fever has been strengthened by the " barrack epidemics " these occur when adolescents are collected and crowded together, and present a regular cycle in which an epidemic of streptococcal tonsillitis is followed after a latent interval by an outbreak of rheumatic fever Recruits are vulnerable when exposed to unaccustomed training and fresh strains of streptococci In these epidemics there is a high carrier rate for the streptococcus The author quotes a number of reports of barrack epidemics, and emphasizes the damage they do among recruits for the Services, so many of whom, once they have acquired the infection, have to be " invalided out "

The war of 1939–45 affected the civilian population to an unprecedented extent, but nevertheless the decline in incidence of rheumatic fever continued and reached a new low level in 1942, when the crude all-age death rate sank to 12 1 per million—scarcely one-half of what it was in 1934 Figures are given of the decline in incidence in Cardiff, Bristol, Leicester, and Glasgow Military experience showed a similar decrease in the incidence and severity of cases of rheumatic fever A comparison is made of the numbers of Service patients treated in military and E M S hospitals, and the proportion of patients suffering from rheumatic fever among all those with " rheumatism " appeared to be approximately the same in both types of hospital It seems that the number of men invalided from the Services for rheumatic fever has steadily declined through recent wars

The author discusses chemoprophylaxis, but points out that good ventilation and the avoidance of overcrowding are still the most important methods of preventing outbreaks of streptococcal disease He quotes Cruickshank (*Mon Bull Min Hlth*, 1946, 5, 144), who says that while sulphadiazine prophylaxis seemed to help to control streptococcal epidemics, it had an unhappy sequel in the appearance of sulphonamide resistance in certain strains of the organism, and that prophylactic use of sulphonamide drugs might be limited to children who have had 2 attacks of rheumatic fever or have had 1 attack accompanied by carditis

W Tegner

Laboratory and Clinical Criteria of Rheumatic Carditis in Children L M Taran *J Pediat*, 29, 77–89, July, 1946

The essence of this paper is an assessment of the value of the various diagnostic criteria as a measure of continued activity in rheumatic carditis

A group of 200 boys and girls, ranging in age from 6 to 14 years, was studied. They were observed from the beginning of an attack of rheumatic carditis to the end of the active process and for at least 6 months after this. The only treatment was good nursing, balanced diet, and moderate amounts of synthetic vitamins. Occasionally the patient was given small doses of salicylates for arthralgia. In each case a complete clinical and laboratory examination was carried out as well as a cardiographic and immunologic investigation.

Leucocytosis—One out of 10, no leucocytosis at all, 9 out of 10, continued leucocytosis for the first 2 weeks, 7 out of 10, continued leucocytosis at end of fourth week. At the end of 7 weeks there was no leucocytosis in any case. All cases with a leucocytosis showed clinical rheumatic activity, and 9 out of 10 continued to show clinical rheumatic activity when the leucocytosis had disappeared.

Fever—Fever as a manifestation of cessation of rheumatic activity is not borne out in this series, the average febrile period was 6 weeks.

A-V Conduction—In this series a prolonged P-R interval in a rheumatic child in the absence of other laboratory or clinical evidence was not found a safe index of continued rheumatic activity, and the return to a normal conduction time did not always mean cessation of activity.

Pulse Rate—This was found to be an adequate index of cessation of activity. There was no correlation between pulse rate and temperature. The rate was highest during the first 3 weeks of the disease and was as high as 140, and no case showed a drop to below 100 before the end of the ninth week.

Sedimentation Rate—This was found not to be as reliable a guide as is commonly believed. Many cases showed a still active rheumatic condition with a normal sedimentation rate. At the end of 16 weeks a number of cases with no clinical evidence of activity had a slightly elevated sedimentation rate.

Weight Gain—This also was not found to be an index of quiescence. At the end of $7\frac{1}{2}$ months all the children had reached a normal weight gain level, yet 40 per cent still showed mild rheumatic activity.

Hæmoglobin—All cases showed a moderately severe anæmia to start with, the hæmoglobin ranging from 7 to 9 g, in 2 children it was as low as 5 g. It was only after 32 weeks that all the cases returned to 12 5 g or more. However, 40 per cent still showed clinical rheumatic activity after the hæmoglobin was normal.

Vital Capacity—In this series vital capacity proved to be the most sensitive single index, all the children having a vital capacity of 40 per cent or less below normal for age and body surface. None reached the normal again until 16 weeks after the onset of the carditis. This index also failed as a specific diagnostic measurement because some children continued to have clinical evidence of disease although the vital capacity was normal.

The relation between clinical activity and various tests is indicated in a table. The author points out that active rheumatic disease must be suspected when there is a tendency to fatigue without cardiac insufficiency, emotional instability, and marked pallor. Tachycardia with a tumultuous rhythm, and a gallop rhythm with rapid or slow cardiac rate are looked upon as evidence of rheumatic carditis, and their absence as auscultatory evidence that carditis is at an end. However, the author finds that these criteria are inadequate in diagnosing mild smouldering carditis. *Richard Sands*

Significance of Downward T Waves in Precordial Leads of Normal Children. E. GOLDBERGER *Amer J Dis Child*, **71**, 618–621, June, 1946

Goldberger took electrocardiographs in 50 children, aged 5 to 11 years, who were regarded as normal from the cardiac point of view. He used a unipolar præcordial electrode in 6 positions from the right of the sternum to the mid-axillary line, i e leads $V_1–V_6$. In 9 children (18 per cent) T was inverted in lead V_4—i e with the electrode in the fifth left interspace in the mid-clavicular line. He found that when the QRS complex shows an RS pattern, which is usual when the electrode is placed to the right of the left mid-clavicular line, T may be inverted or upright. But when QRS shows a QR or a QRS pattern, as is usual in leads V_5 and V_6, T is upright. An inverted T in association with a QR pattern is stated to be always abnormal. The RS pattern, with which the inverted T may be associated, is believed to occur when the præcordial electrode is facing the epicardial surface of the right ventricle, and the QR and QRS patterns when it is facing the epicardial surface of the left ventricle, hence the larger area of the præcordium which will normally give an inverted T in the child as compared with the adult, the right ventricle being relatively larger in the child. *Harold Cookson*

Peripheral Blood Flow, Rectal and Skin Temperature in Congestive Heart Failure. The Effects of Rapid Digitalization in this State. H J STEWART, W F EVANS, H BROWN, and J R GERJUOY *Arch intern Med*, **77**, 643–658, June, 1946

This paper describes an attempt to measure the total peripheral blood flow in patients with congestive cardiac failure before and after the intravenous administration of strophanthin-K and digitaline (Nativelle). Fifteen patients were admitted to hospital and placed at complete rest in bed. Fluid intake was limited to 1,200 ml daily and salt intake to 3 g. Before administration of the drug four sets of observations of rectal and skin temperatures were made from which three control levels of peripheral blood flow could be estimated. Blood pressure, heart rate, basal metabolic rate, circulation time, and venous pressure were also estimated. Beginning 15 minutes after the injection, the authors repeated the observations at 20-minute intervals for 70 to 180 minutes. The data collected both before and after the injections were averaged. Strophanthin-K

was given intravenously in doses of 0 25 mg except to those patients with mitral stenosis, to whom 0 125 mg was given Digitaline (Nativelle) was given in doses of 1 2 mg Some patients had normal rhythm, others auricular fibrillation

The average peripheral blood flow for all patients with heart failure was 32 ml per square metre per minute as compared with 33 ml for normal subjects Both rectal temperature and average skin temperature were higher than in normal subjects

The effect of strophanthin and of digitaline was to increase considerably the peripheral blood flow, to increase the average skin temperature, and to decrease the rectal temperature The heart rate was slowed, the circulation time shortened, and the venous pressure lowered The authors point out that other workers have shown that digitalis in heart failure produces a decrease in the size of the heart and an increase in cardiac output Thus, during heart failure the volume of blood allotted to the peripheral circulation in unit time is in the normal range, but it moves so slowly in a distended vascular bed that it is insufficient to eliminate heat from the body and the rectal temperature rises After the exhibition of strophanthin-K the peripheral blood flow increases, the skin temperature rises, and the rectal temperature falls The highest peripheral blood flow following the administration of strophanthin-K occurs after 64 minutes, and that following the administration of digitaline (Nativelle) after 114 minutes   *Geoffrey McComas*

Electrocardiographic Features of Myocardial Infarction as Affected by Involvement of the Septum and by Complete and Incomplete Transmural Involvement [In English] H E B PARDEE and M GOLDENBERG *Arch Inst Cardiol Mexico*, 16, 109–130, May 31, 1946

The post-mortem findings in 12 hearts were correlated with the electrocardiographic findings in leads I, II, III, IV F Two anterior wall infarcts with septal involvement but without involvement of the sub-epicardial fibres showed a QS deflection (absent R wave) in IV F, a feature usually attributed to involvement of those fibres The QS deflection was associated with septal involvement, as in 5 anterior wall infarcts (4 with no sub-epicardial involvement) it was absent in the only one without septal involvement In 3 of the 4 cases without sub-epicardial necrosis, ST- and T-wave changes in the limb leads were similar to those seen after anoxaemia and exercise tests In the fourth case typical changes of acute anterior infarction were seen in all 4 leads Two complete posterior wall infarcts with septal involvement had typical acute ST- and T-wave changes in all 4 leads Two posterior wall infarcts, without sub-epicardial and septal involvement, failed to show typical changes in any lead Typical ST- and T-wave changes were only found in lesions involving the septum and adjacent anterior or posterior walls Complete transmural involvement of the posterior wall was the only constant pathological finding in cases with large Q 3

Of 6 incomplete mural infarcts only 1 had a typical record of anterior or posterior wall infarction
     W T Cooke

Coronary Occlusion in Young Adults Review of Fifty Cases in the Services M NEWMAN *Lancet*, 2, 409–411, Sept 21, 1946

In view of the apparent rarity of coronary occlusion in young adults records were analysed of 50 Service men and women up to the age of 35 who had been invalided with, or had died from this condition In 39 cases proof of coronary occlusion was obtained at necropsy, and in the surviving cases the diagnosis was supported by the characteristic cardiographic changes The youngest patient was aged 20, and 22 of the 50 were in their twenties, as in the older age groups, the frequency increased with age Coronary occlusion appears commoner in males than females in the younger age groups as well as in the older

The striking feature was tne good physical development and nourishment of these subjects, robustly built, they had a tendency to adiposity Forty-five had been grade 1 on entry The heart had been recorded as normal in every case, and all the subjects were apparently in excellent health

Only 3 showed evidence of hypertension Previous infection may have been of ætiological significance in a few cases , 3 gave a history of rheumatic fever, 2 of scarlet fever, and 1 (with marked coronary atheroma) had chronic osteomyelitis, 2, who both survived, had syphilis In more than half there was no evidence of physical strain before onset, and less than half had done heavy work in their pre-Service occupation

The 78 per cent mortality, 83 per cent of which was immediate, was surprisingly high, and would appear to indicate a much worse prognosis in younger people At necropsy the left coronary artery was affected in 17 cases, the right in 5, and both in 16 The findings did not support the view of Leary (*Arch Path*, 1941, 32, 507) that calcification does not occur in the younger age group, and that coronary occlusion is due to sub-endothelial fibrosis with necrosis of the intima leading to thrombosis Only 2 cases showed fibrotic reaction without calcification, the remaining 37 presented the usual degenerative atheromatous changes of coronary disease in older persons, several with extensive calcification In 29 of the 39 cases no thrombus was found, half the cases showed recent or long-standing infarcts

[The findings and conclusions are similar to those of Miller and Woods (*Brit Heart J*, 1943, 5, 101) who, however, noted a striking history of familial " defective tubing "]
     E G Sita-Lumsden

Haemodynamic Factors and Retinal Changes in Hypertensive Diseases [In English] S BJÖRK. *Acta med scand* Supp 173, 1–165, 1946

WARDROP GRIFFITH (in uniform) and THOMAS LEWIS during the 1914–18 war

THOMAS WARDROP GRIFFITH

Professor Wardrop Griffith can only have been known personally to few members of the British Cardiac Society, as it is sixty years since he became Professor of Anatomy in the Yorkshire Medical School at Leeds and he flourished as a physician in the generation between those of Clifford Allbutt and of the present most senior physicians in Leeds

Wardrop Griffith was born in 1861, the tenth child and eighth son of Charles Fox Griffith, J P , of Aberdeen He was educated at the Aberdeen Grammar School, and the University of Aberdeen, where he qualified in April 1882 with the highest honours After qualification he acted as demonstrator in anatomy to John Struthers for four terms, and under that master got a thorough training in dissecting-room anatomy

In October 1883 he took the post of house physician at Leeds General Infirmary, and the next year was appointed the resident medical officer This post he retained until his appointment as Professor of Anatomy in the Yorkshire College in Leeds in 1887 As this was a part-time Chair, Griffith put up his plate in Park Square, and started practice as a physician In 1892, in addition to his professorship of anatomy, he was appointed an honorary assistant physician at the Leeds General Infirmary In 1904 he was elected physician in charge of outpatients, and became a full honorary physician in 1905, from which post he retired in 1925 He held the Professorship of Anatomy up to the year 1910, when he became Professor of Medicine, he resigned the chair in 1925, when he retired from the Leeds Infirmary.

Wardrop Griffith made a great reputation as a teacher of anatomy Despite the fact that he obtained the chair at the early age of 26 years and also that it was a part-time post, he took the School of Anatomy at Leeds to the front rank, both by the thoroughness of his work and his brilliance as a lecturer As pointed out by an old student in the Yorkshire Post on October 29, 1946, " He was a pupil of the great John Struthers, and inherited from him an exact and lucid conception of anatomy, and a great power of elucidating much of its mysteries He was a man who impressed students, and no student ever played the fool at his lectures His presence in the dissecting room was always welcome, and his demonstrating powers were of a high order " He had examined in Anatomy in the Natural Science Tripos and the 2nd M B examination at Cambridge

There was something of the dramatic in Griffith's teaching, of which those of us who heard him talk in the Cardiac Society and at the Association of Physicians were well aware In his anatomical lectures he was wont to jump on to a table to illustrate the action of muscles and joints, and was wont to perform other acts of pantomime His students, when they came together in after years, took pleasure in recalling their memories of Wardrop Griffith, chiefly as a teacher of anatomy with his little mannerisms, his punctuality, and his kindliness

While holding the Chair of Medicine, his lectures were equally lucid and thorough, and his teaching at the Infirmary was very sound, but it is doubtful whether he ever produced quite the same atmosphere as obtained at his lectures in anatomy Griffith was extremely assiduous and punctual in all his hospital and university duties, and expected punctuality from others as well He identified himself very closely with the Leeds Medical School, and so great was his share in this, that it was said that, " he personally supervised the laying of every brick " As Dr Veale stated, while presenting Griffith for the Honorary D Sc in 1929, " There is little over-statement in this, for the University owes him a lasting debt of gratitude for the careful planning and sound construction of this building, which now, though being substantially enlarged, still remains a lasting memorial of his efforts "

In the clinical school he founded the clinic for diseases of the skin, and was one of the first to make use of the graphic methods of cardiovascular investigation suggested by the work of James Mackenzie and Thomas Lewis

Wardrop Griffith was one of the original members of the Cardiac Club when it was founded in 1922, and in the early years was very regular in his attendance, and could always be relied upon to give an authoritative opinion on any anatomical question   In 1924 he opened a discussion on the heart in pneumonia   He was, however, already getting senior and most of his active writing had already been done so that he was elected an Extra-Ordinary Member as long ago as 1928   In the third volume of *Heart* he published an exhaustive paper on two cases of heart block, in which he noted the ausculatory phenomenon of auricular beats   He gave the Schorstein lecture on some cardiac problems in 1912   He was a critical worker and Thomas Lewis gave much importance to his opinion, and often submitted work for his criticism   In Griffith's home circle, " Thomas Lewis " became a family saying, meaning he was thinking about something else!

Griffith had taken the M R C P in 1901 and was elected F R C P in 1908   He served on the Council of the Royal College of Physicians from 1924 to 1926   He acted as examiner in Medicine in the Universities of Cambridge and Manchester   In 1922 his own University of Aberdeen conferred upon him its Doctorate of Law, and Leeds University conferred upon him the Honorary Degree of Doctor of Science

Tall, well proportioned, and good looking, there was a certain charm of manner in Wardrop Griffith, which made him very approachable to younger members of the profession, and he was a real friend to all the early members of the Cardiac Club, and was intensely interested in any work that any of them were doing   His memory was prodigious, and he could reel off pages of poetry chiefly of the lighter kind such as Gilbert and Sullivan, Bab Ballads, etc   He was an authority on the Waverley novels, and knew the stories and characters well   He had also the same intimate knowledge of Dickens and Thackeray

During the War of 1914–18, Wardrop Griffith served with Number 2 Northern General Hospital at Beckett's Park, Leeds, and in 1918 was appointed C M G   From 1918–27, he represented the University of Leeds on the General Medical Council

Being one of ten children, he always kept in touch with the remaining brothers and their children   his two sisters died fairly early in life   The evening of Wardrop Griffith's life was saddened by the loss of his wife in 1937, and the gradual loss of his eyesight, so that he was unable to read for the last three years

We mourn the loss of our most senior member, whose youthful outlook on medicine kept him in touch and sympathy with his junior colleagues long after he had retired from the active staff of the Leeds Infirmary, at a time when his great clinical experience and critical outlook was most helpful

<div style="text-align: right">W   E   HUME</div>

Thirteen years ago, when I attended the meeting of the Cardiac Club at Leeds, I have a clear memory of Wardrop Griffith of the distinguished way he presided over the meeting, of his lucid demonstration of specimens of congenital heart disease, and of his kindness to me a very junior member of the Club   It has, therefore, been a great pleasure with the help of John Towers, compiling this bibliography of his publications on cardiology   His first paper, in 1889, written for his M D thesis, was on 50 cases of empyema, but very soon he had started his interest in congenital heart disease   His remaining papers dealt mainly with other anatomical abnormalities and with nervous diseases

<div style="text-align: right">MAURICE CAMPBELL</div>

Remarks on fifty consecutive cases of empyema occurring in the medical wards of the general infirmary at Leeds   *Med Chron* (1888–9), **9**, 441

A case of transposition of the thoracic and abdominal viscera, with congenital malformation of the heart and of the arterial and venous systems   *J Anat & Physiol* (1891–2), **26**, 117

Heart with imperfection of the septum of the ventricles and other anomalies   *Proc Anat Soc Gt Brit & Ire* (1896–7), p 18

Example of a large opening between the two auricles of the heart unconnected with the fossa ovalis.   *J Anat & Physiol* (1899), **33**, 261

Obstruction of the inferior vena cava   *J Anat & Physiol* (1899), **33**, 503

Specimen of great redundancy of the fossa ovalis   *J Anat & Physiol* (1899), **33**, 502

Two examples of moderator band in the left ventricle of the heart   *J Anat & Physiol* (1899), **33**, 31

Remarks on aneurysm of the coronary arteries of the heart   *Brit Med J* (1931), **1**, 266

Abnormalities of the heart   *J Anat & Physiol* (1902), **36**, 26

A case of almost complete absence of the auricular septum and other cardiac malformations complicated by acquired mitral disease   *Med Chron* (1903), **37**, 385

An example of a peculiar malformation of the tricuspid valve of the heart   *J Anat & Physiol* (1903), **38**, 251

Note on a second example of division of the cavity of the left auricle into two compartments by a fibrous band   *J Anat & Physiol* (1903), **37**, 255

On affections of the tricuspid valve of the heart, with a note on a pedunculated thrombus occurring in the right auricle   *Edin Med J*, *N S* (1903), **13**, 105

Infective endocarditis involving the pulmonary valves and associated with imperfection of the inter-auricular septum   *Lancet* (1906), **11**, 973

On a case of combined disease of the mitral, aortic, and tricuspid valves of the heart, in which the patient was under observations for 25 years   *Lancet* (1907), **2**, 1147

Unusual diseases of the heart   *Brit Med J* (1909), **2**, 142

Venous pulse in neck   *Brit Med J* (1909), **1**, 720

(with A E Cohn) Remarks on the study of a case showing a greatly lengthened a–c interval with attacks of partial and of complete heart block.   *Quart J Med* (1910), **3**, 126

Remarks on two cases of heart block   *Heart* (1911–12), **3**, 143

The Schorstein lecture on some cardiac problems   *Brit Med J* (1912), **11**, 913

(with A M Kennedy) A case of complete auriculo-ventricular heart block with a report of the pathological condition of the heart   *Brit Med J* (1913), **1**, 1203

A presidential address on the development of our knowledge of the diseases of the heart   *Lancet* (1913), **11**, 1517

(with A M Kennedy) Supplementary note on a case of heart block, with an examination of the auriculo-ventricular junctional tissue   *Heart* (1914–15), **6**, 37

Remarks on a communication between the two ventricles of the heart occupying an unusual situation   *Lancet* (1915), **1**, 59

Two cases of patency of the ductus arteriosus   *Quart J Med* (1915), **8**, 191

Embolic aneurysm of peripheral arteries   *Lancet* (1920), **11**, 374

A clinical study of three cases of heart block   *Brit Med J* (1921), **1**, 763, and 956

(with J Hay *et al*) Discussion on cardiac irregularities especially in reference to prognosis and treatment   *Brit Med J* (1924), **11**, 697

CHARLES HERAPATH

Charles E K Herapath was born in Bristol in 1882, and was the son of a well-known and beloved general practitioner   He was educated at Clifton, at University College, Bristol, and at the Bristol Royal Infirmary   After qualifying M B , B S , in 1907, he held various house appointments and completed his studies in London, taking the M D in 1910   On returning to Bristol he was appointed to the staff of the Bristol Dispensary but maintained his connections with the Royal Infirmary   He joined the Territorials and became one of the keenest and most efficient officers in his unit   He enjoyed the army drill and discipline and was almost an authority on army regulations which appealed to his precise and accurate mind   During the 1914–18 war he served throughout as a company medical officer, was awarded the M C , and earned the lasting esteem of his men

On his return from war service he was appointed Assistant Physician, and later Physician, to the Bristol Royal Infirmary and here he developed his interest and enthusiasm in cardiology   His attraction in this branch of medicine was probably partly due to his love of mechanical " gadgets " and the consequent appeal of Mackenzie's polygraph   It was the same mechanical bent that made him an enthusiastic motor cyclist at a time when every expedition on a motor cycle was something of an adventure   As a result of his early work with the polygraph one of his main interests in cardiology was the study of the arrhythmias and his long records of patients with heart block and Stokes-Adams syndrome will be remembered   He was probably never happier than when struggling to correct some minor defect in his electrocardiograph or puzzling out some obscure cardiac arrhythmia

Herapath was elected a member of the Cardiac Club in 1924 when it met at Bristol under the chairmanship of Carey Coombs   He attended the meetings regularly but did not give many communications, though in 1932 he was asked to open the discussion on the heart in influenza

Apart from cardiology his other great interests were freemasonry, stamp-collecting, and music   The advent of wireless and the consequent possibility of listening to first-class music in the comfort of his own home was a great delight to him   Herapath was supremely happy in his home and marriage, but he was a rather shy man and not one who made friends readily, and as a result had few intimate companions   However, once the superficial reserve was penetrated it would be impossible to find a more loyal or staunch friend

During the last years of his life he looked forward to retiring to a small house in the country, and it was a great tragedy that his death should occur so shortly after he acquired a house and garden at Keynsham, in which he was taking such a great delight

He leaves a widow, one daughter, and one son who is, at present, a medical student

<div align="right">C BRUCE PERRY</div>

Auricular fibrillation   *Bristol med -chir J* (1911), **29**, 148

(with H Waldo) A case of complete heart block, with post-mortem examination   *Lancet* (1922), **1**, 271

(with C F Coombs) Auricular failure   *Bristol med -chir J* (1923–24), **41**, 180–201

(with C F Coombs) The three chief types of cardiac failure   *Clin J* (1926), **55**, *529*

Changes in ventricular rate associated with Stokes-Adams attacks in complete heart block   *Lancet* (1926), **1**, 653

Auricular flutter   *Brit med J* (1928), **1**, 213

(& C B Perry) Coronary arteries in case of familial liability to sudden death   *Brit med J* (1930), **1**, 685–687.

PAROXYSMAL TACHYCARDIA FOLLOWED BY TEMPORARY INVERSION OF THE T WAVES

BY

R. E STEEN

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It is now generally recognized that inversion of T waves such as is met with in coronary disease can occur in a number of other conditions also, for example, in myocardial disease due to toxæmia or hypertension, from large doses of digitalis, from the physiological effects of taking cold drinks, as a result of the position of the heart, and even from changes of posture especially in persons of the neuro-circulatory asthenic type

Attention has, however, only recently been given in the literature to the fact that electrocardiographic features simulating serious coronary disease may in certain cases occur as a transient feature after paroxysmal tachycardia   The condition, furthermore, is of more than mere academic importance, since if not recognized, an erroneous diagnosis of coronary disease may easily be made especially if the attack of paroxysmal tachycardia passes unnoticed or is thought to have been an acute coronary lesion   Either these changes after paroxysmal tachycardia are very rare or it would seem possible that cardiologists have been familiar with their occurrence but have not recorded them

White *et al* (1941) in a review of various conditions other than organic disease causing inversion of the T wave in lead II makes no mention of paroxysmal tachycardia, and in a search of British and American papers only eighteen previous cases appear to have been described   Graybiel and White (1934) reported two cases of paroxysmal ventricular tachycardia in young robust adults, one followed by inverted T I and the other by inverted T II and T III, there was no sign of organic disease, and there was a gradual return to a normal cardiogram   Campbell and Elliott (1939) described two cases of paroxysmal tachycardia, one being ventricular, that gave transient changes simulating coronary thrombosis one of these gave a history of diphtheria, and the other was of long standing and had been suffering from increasing dyspnœa during the intervals between attacks, both died at a later date Though these two cases differ in their organic nature from the other cases described and from the present one, which except for the electrocardiographic abnormality seemed normal in other respects, Campbell and Elliott nevertheless laid stress on the transient nature of the cardiographic changes following the tachycardia   Cossio, Sabathie, and Berconsky (1941) described four cases, and Campbell (1942) a further three cases that were clinically benign Currie (1942) described a further case probably of ventricular origin in a girl aged thirteen, followed by inversion of T waves, and a return to a normal cardiogram in one month   Dubbs and Parmet (1942) added a further case, Geiger (1943) one case, Zimmerman (1944) three cases, and Ward (1946) one case   The present case was one of paroxysmal auricular tachycardia and was clinically benign

PRESENT CASE

A woman, aged 27, was admitted to the Meath Hospital, Dublin, on February 16, 1945. The history was that quite suddenly when she was walking three days previously her heart began to beat very heavily and she found her breathing became difficult   She also felt inclined

to vomit but was unable to, and experienced a throbbing sensation in her throat   She stated that she had a similar attack but milder in character a year previously.   There was nothing of importance in the family history   Physical examination was normal except for some bad teeth, the rapid heart action, and a suspicion of œdema in her legs.   The heart rate was extremely rapid and regular so that it was impossible to estimate the rate of the pulse at the
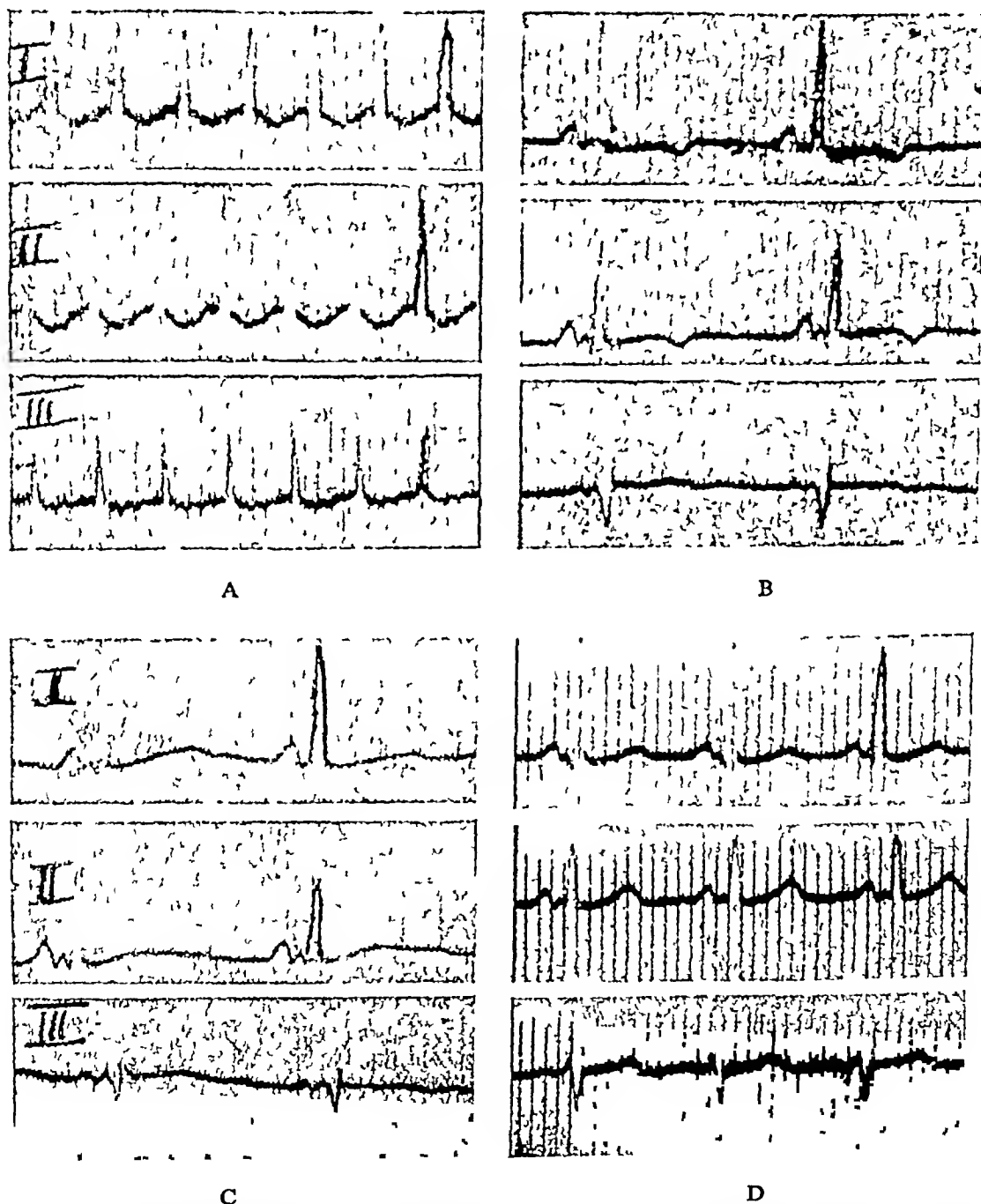

A

B

C

D

Fig 1 —(A) Paroxysmal auricular tachycardia (16/2/45)   (B) Inversion of T I and T II six days after cessation of attack (24/2/45)   (C) More normal appearance of T I and T II two days later (26/2/45)   (D) Completely normal T I and T II sixteen months later (20/6/46)   In each case one complex has been inked in to mark it more clearly

wrist, but when taken at the apex beat by auscultation it was found to be approximately 240 a minute, a figure that actually agreed with the rate as timed on the electrocardiogram The method of tapping with the foot synchronously with the sound as heard on auscultation advised by Levine for timing cases of rapid heart action was found helpful in this case as otherwise it would have been very difficult to time at all accurately the extremely rapid heart rate

Attempts to control the rapid heart action by the ordinary simpler methods were unsuccessful but the attack finally stopped between 7 a m and 1 p m on the morning of February 18, 1945, after 24 grains of quinidine sulphate had been given, spread over a period of 36 hours, the attack having lasted in all approximately four-and-a-half days All other investigations both cardiological and otherwise were negative, including the Wassermann reaction

Subsequent convalescence was uneventful except that the patient complained that she had a very slight attack on February 26 which she stopped herself by ocular pressure The patient was discharged on March 21, 1945

The electrocardiograms demonstrate the transient occurrence of inversion of T waves in leads I and II Fig 1A on February 16, the day of admission, shows typical paroxysmal auricular tachycardia Fig 1B on February 24, six days after the cessation of the attack, shows typical inversion of T I and T II Fig 1C taken on February 26, two days later, shows the T waves no longer inverted Fig 1D on June 20, 1946, sixteen months later when the patient felt perfectly healthy except that she was pregnant at the time, shows a normal cardiogram

DISCUSSION

The importance of not confusing a benign condition like the above with serious cardiac disease has already been stressed It is of interest to consider the possible aetiological factors that may play a part in producing the abnormal electrocardiographic findings Clearly even if the condition is less rare than it would seem, only a small minority of cases of paroxysmal tachycardia are associated with the abnormal type of cardiogram Campbell suggests two possible explanations (1) " chemical or other changes in the myocardium as a result of a prolonged attack " and adds that " in this sense the changes would, to some extent, be a measure as to the severity and seriousness of the attack, and might indicate the need for adequate rest " or (2) " that it depends on changes in the position of the heart, and that as the diaphragm sinks, or as the stomach empties, the heart returns to its more normal position with the return to its normal electrocardiographic pattern " While he mentions in support of this view that it would bring the case into line with some of the other T wave changes reported from alterations in the position of the heart, he is inclined to discount this latter theory from the fact that the time taken for recovery from the electrocardiographic changes is measured in days rather than in hours He sums up his views by saying that the condition " does not indicate any organic disease, but is a completely reversible process indicating some degree of exhaustion or strain of the heart muscle " The title of his paper " Inversion of T waves after long paroxysms of tachycardia " suggests that one of the most dominant factors is the length of the attack, and Currie also refers to this causative factor in support of which was the fact that in his case the changes in the cardiogram were less in an attack of short duration compared with one of longer duration. In the present case the attack lasted probably between four and five days and duration may have been a factor in the changes, but it is also worth noting that the rate of 240 a minute is an exceptionally high one, and since rapid heart action is well-recognized as a strain on the heart, it is possible that in this case the high rate of striking may have played an important part in determining the cardiographic changes That such changes should occur is not surprising when one remembers that pulsus alternans and anginal pain are quite commonly experienced in paroxysmal tachycardia of

benign type, and that inversion of the T wave in lead I is considered as the cardiographic equivalent of pulsus alternans in cases of coronary disease

From the practical point of view it is hoped that by the recording of this and other cases, otherwise healthy people may be prevented from being condemned to a life of cardiac invalidism

SUMMARY

A case of paroxysmal tachycardia with temporary inversion of T waves in leads I and II is reported   This brings the total number of such cases published in British and American journals to nineteen.   Stress is laid on the possible influence of the very high rate of tachycardia in this particular case as an ætiological factor in the electrocardiographic changes   The ease with which these changes may be confused with coronary disease is emphasized

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THE EFFECT OF DEMEROL, ERGOTAMINE, AND DIHYDRO-ERGOTAMINE ON MORTALITY AFTER CORONARY OCCLUSION IN DOGS

BY

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In a previous report (Manning *et al*, 1939) it was shown that fatal ventricular fibrillation occurred in 75 per cent of untreated conscious dogs following sudden occlusion of the left circumflex branch of the left coronary artery   This mortality can be reduced to 10 per cent by bilateral sympathetic denervation of the heart before ligation (McEachern *et al*, 1940) It has also been shown that coronary dilator and anti-spasmodic drugs are effective, but to a lesser degree, in reducing this mortality (McEachern *et al*, 1941, Le Roy *et al*, 1941, 1942, Gilbert, 1942)   These results have been confirmed by Gilbert and his associates whose further work supported the suggestion that a reflex coronary spasm initiated by the occlusion resulted in a generalized myocardial ischæmia which led to the fatal sequence of events (McEachern *et al*, 1940, Le Roy *et al*, 1941, 1942, Gilbert, 1942)   It was also pointed out that sympathetic denervation may have rendered the myocardium less susceptible to the onset of ventricular tachycardia and fibrillation initiated by the infarction, rather than by interruption of a reflex arc (McEachern *et al*, 1940)   Possibly, both types of mechanism were present

In view of these findings and the work of others (Leriche *et al*, 1931, Miller, 1939, Evans, 1940, Katz and Joachim, 1939, 1945, Falk, 1942, Gregg and Shipley, 1944, 1945, Orth, 1946, and Harris, 1946), it was considered advisable to investigate the effect of sympathetic inhibiting agents, using the same experimental conditions and procedure previously described (Manning *et al*, 1939)   For this purpose ergotamine tartrate (Gynergen II, Sandoz) was used and also a new ergot derivative, dihydro-ergotamine (DHE-45, Sandoz)

Stoll and Hoffman (1943) have prepared a crystalline alkaloid derivative by hydrogenation of ergotamine which is less toxic and exerts a sympathetic inhibiting action stronger than ergotamine (Rothlin and Brugger, 1945)   Dihydro-ergotamine lowers the blood pressure and slows the heart rate in the narcotized cat and rabbit   It is reported that DHE-45 acts on effector organs in such a way as to render them indifferent to sympathetic impulses

Orth (1946) found that 0 4 mg/kilo prevented cyclo-propane-epinephrine induced ventricular fibrillation in the dog   Using rats it was demonstrated that the oxytocic effects did not occur   Gangrene in the rat's tail was rarely produced following large injections of DHE-45 for more than thirty days   The dose recommended by Orth is approximately twice the dose of ergotamine tartrate for the prevention of cardiac effects due to cyclopropane and epinephrine   The protection lasted for about one hour and the epinephrine reversal of blood pressure in anæsthetized dogs did not occur

Clinical reports have indicated that DHE-45, in doses of 1 mg intramuscularly, is as effective as ergotamine tartrate in the relief of migraine (Horton *et al*, 1945)   It did not produce the disturbing side effects of other ergot preparations and in this dosage it had no demonstrable effect on the uterus, heart rate, blood pressure, peripheral arterial pulsation, or on the temperature and colour of the extremities (Horton *et al*, 1945, and Hartmann, 1945)

In view of the results previously obtained (McEachern *et al*, 1940, Le Roy *et al*, 1941, 1942, Gilbert, 1942, Falk, 1942, Swanson, 1945, Mokotoff and Katz, 1945, Gerger, 1945, and Lindner and Katz, 1941) with coronary dilator or antispasmodic drugs, it was considered advisable to include in this study a small series of experiments with demerol   The hydrochloride of the ethyl ester of methyl-4-phenylpiperidine-4-carboxylic acid (demerol), discovered in 1939 in Germany (Gruber *et al*, 1941, and Hori and Gold, 1944), is said to possess antispasmotic or parasympathetic-depressent, analgesic, and sedative effects and has been used clinically for this purpose with some degree of success (Hori and Gold, 1944, and Flatt, 1946)

METHODS

Seventy-two normal dogs were used in these experiments   At operation a loose ligature was placed around the left circumflex branch of the left coronary artery close to its origin as described in a previous report (Manning *et al*, 1939)   The free ends of the loose ligature were brought out of the chest at either end of the skin incision and the chest closed in layers   A sterile dressing protected both the skin incision and the free ends of the ligature   The following day (24 hours later) ligation was effected by traction on the loose ends of the ligature

Three groups of experiments were carried out using demerol, ergotamine tartrate, and dihydro-ergotamine   In addition, 8 dogs were ligated without the use of drugs, as a check on our technique and the mortality rate in conscious dogs, and to increase the original control series   In all cases the drugs were given before the ligation   Electrocardiograms were taken before and after the administration of the drug, before, during, and for 30 minutes after ligation and then intermittently for some time after the occlusion   The animals were observed clinically and with the electrocardiograph for the 24-hour period   An autopsy was performed immediately on all animals that died

As previously described (Manning *et al*, 1939) "sudden death" for the purpose of these studies, means death within the first 24 hours   This period for mortality figures on sudden death following coronary occlusion was adopted by us and by others (Le Roy *et al*, 1941, 1942, and Gilbert, 1942) because most of the animals that fail to survive, succumb shortly after the occlusion (Table I) and up to the present time these studies have been primarily concerned with the immediate mortality following sudden coronary occlusion   Although long-term studies have not been carried out, it has been observed that if the animal survives the 24-hour period it is unlikely that a cardiac death will occur (Manning *et al*, 1939, and McEachern *et al*, 1940)

RESULTS

Control Group   Six of the 8 dogs in which the left circumflex branch was occluded died within the first 24 hours   The sequence of events, including the cardiographic changes, was found to be the same as previously described (Manning *et al*, 1939, and Le Roy *et al*, 1941, 1942)   In 4 animals ventricular tachycardia and terminal ventricular fibrillation occurred within the first 10 to 12 minutes (Fig 1 on page 93)   Two animals were found dead in 12 to 18 hours following the ligation and the remaining 2 survived   This agrees closely with our earlier results and the findings of others when the left circumflex branch is suddenly occluded in the normal conscious dog   Including the former control series of 16 dogs, the mortality for the untreated group was 18 deaths out of 24 dogs within the first 24 hours, or 75 per cent

Demerol Series   In these experiments 12 dogs were used   Demerol was given intramuscularly in doses of 10 mg /kilo followed by a second injection of 5 or 10 mg /kilo intravenously 15 to 25 minutes later   Ligation of the left circumflex was carried out in the manner described 10 to 20 minutes following the second injection of demerol

The sequence of events following occlusion was similar to that seen in the control group except that the animals appeared somewhat more disturbed   The incidence and nature of

TABLE I
RESULTS
Showing comparison with previous studies and with those of Le Roy *et al*, 1942

Experimental group	Number of dogs	Immediate mortality		24-hour mortality (percentage)
		Time (min)	Percentage	
Control	24	10–12	50	75
Demerol	12	2–4	58	58
Ergotamine tartrate	13	15	15	70
DHE-45	23	2–12	13	30
1 { Bilateral cardio-sensory denervation	22	9–15	9	9
Papaverine	20	17	45	50
Quinidine	20	5	45	55
2 { Control	13	—	—	70 } Light anaesthesia
Xanthine treated	39	—	—	38
Theobromine treated	21	—	—	23
Theophylline treated	18	—	—	56
Atropine treated	8	—	—	34
Atropine	4	—	—	50
Theophylline and atropine	6	—	—	53

1 McEachern *et al*, 1940, 1941, Smith *et al*, 1940
2 Le Roy *et al*, 1942

pain after the occlusion was variable, being the same or greater in 3 animals, absent in 1, and somewhat decreased in the remaining 8   Seven animals died in ventricular fibrillation in 2 to 4 minutes following ligation and the remaining 5 survived the 24-hour period

The number of animals used does not warrant a statistical comparison of mortality with the control group   However, it would appear that demerol did not afford much protection against cardiac irregularities, tachycardia, and fibrillation, following sudden coronary occlusion In the cardiogram the effects usually seen following experimental coronary occlusion were observed   There was little or no change in heart rate or rhythm following the injection of demerol   On ligation the typical S-T elevation and T wave changes occurred (Fig 2); extrasystoles were common   The outstanding feature, however, was the rapid onset of the ventricular tachycardia, which occurred in eleven experiments and terminated in fatal ventricular fibrillation within 2 to 4 minutes in 7 of the 12 animals   In the control group ventricular tachycardia and fatal ventricular fibrillation usually occurred about 10 to 11 minutes following ligation   Four of the 5 dogs that survived did so in spite of the rapid onset of ventricular tachycardia (Fig 2 on page 93) which in the control experiments was invariably followed by fatal ventricular fibrillation

Ergotamine Tartrate Series.   In these experiments 13 dogs were used   In the first 2 animals 0 5 mg/kilo ergotamine tartrate was given intravenously   In one of these a severe heart block occurred following the injection of ergotamine and the animal died in fatal heart block 36 minutes after ligation   In view of these effects a dose of 0 25 mg/kilo was given to the remaining 11 dogs   Nine of the 13 animals died within the first 24 hours   Two dogs died shortly after the ligation, one in ventricular fibrillation in 9 minutes and the other in 36 minutes with heart block following the occlusion   The remaining 7 died in periods ranging from 9 to 18 hours, following ligation (Fig 3 on page 94)   Shortly after the intravenous injection of ergotamine tartrate the animals showed marked muscular weakness, most apparent in the limbs   Increased respiration and dyspnœa, which in several was of an asthmatic nature, were prominent features   Salivation was also observed   Vomiting occurred in two and bowel

evacuation in 5 of the 13 animals The generalized muscular weakness and dyspnœa continued following the occlusion Throughout the 24-hour observation period these signs continued and were associated with collapsed peripheral veins and pulseless cold extremities These effects appeared to increase in severity and approached a maximum some 10 hours following the injection and occlusion In the animals that did not survive, death occurred suddenly about this time, in the same manner as was seen in other experiments in which the animals succumbed shortly after ligation In 4 dogs a second injection of ergotamine was given 8 to 10 hours following the ligation, but the terminal event was not delayed any longer

Following the injection of ergotamine tartrate there was a decrease in heart rate in 12 out of 13 dogs In 6 of the animals varying degrees of S-A and A-V heart block occurred (Fig 4) The P-R interval was increased by the drug and the QRS interval showed little or no change In general the QRS complex and T wave showed inconstant variations in amplitude, the T waves being increased in 2 instances, decreased in 4, reversed in 1, and unchanged in the others In 3 experiments the RS-T segment was depressed following injection of the drug

Following ligation there was some increase in the heart rate Extrasystoles were not seen as frequently as in the control group The ventricular tachycardia frequently seen shortly after ligation occurred in only one animal, this progressed to fatal ventricular fibrillation in 11 minutes following ligation One other animal died in heart block (in 36 minutes) which was present even before the ligation Seven of the 9 dogs that did not survive the experiment died in the 12 to 18-hour period following ligation, 1 died in block, 2 in fibrillation, and 4 were found dead in the cage In general, the rhythm became regular within half an hour following the occlusion, but was followed by a progressive deterioration which reached a maximum 12 hours later Wide variations in individual dogs were seen, but the most common findings were varying degrees of S-A, A-V, and bundle branch block An increase in the number of extrasystoles was also noted and auricular fibrillation occurred in 2 dogs, nodal or extrasystolic rhythm occurred in a few and A-V dissociation was also observed In contrast to other groups there was following ligation a progressive depression of the RS-T segment which had returned or was approaching the base line again in about 30 minutes Deeply inverted T waves were also common (Fig 4 on page 94)

It was apparent that ergotamine tartrate in doses of 0 25 mg /kilo was effective in inhibiting the mechanism of fibrillation and so reduced the "immediate" mortality A delayed cardiac death, however, occurred 12 to 18 hours later in 70 per cent of the animals

Dihydro-ergotamine Series In these experiments 23 animals were used DHE-45 was given intravenously (0 4 mg /kilo) 4 to 5 minutes prior to the occlusion In the majority of cases some degree of salivation occurred within 1 to 2 minutes, but was less than that seen in the ergotamine series Gastro-intestinal upsets occurred in 2 instances (retching in one animal and vomiting in another about 3 to 4 minutes following the drug) Bowel movement did not occur before ligation, but was frequent shortly after ligation Respiration was slightly increased by the drug in a few animals as compared with the marked increase and even dyspnœa seen in the ergotamine tartrate series The drug appeared to have little or no effect on the pain of ligation Although most of the animals appeared slightly unsteady following the occlusion, the general collapse and weakness and toxic appearance that was such a prominent feature of the ergotamine series was not apparent Clinically, these animals appeared more like the control dogs that survived the immediate effects of the occlusion Seven of the 23 dogs died within the 24-hour period following ligation (30 per cent mortality) Three of these died within 12 minutes following occlusion in ventricular fibrillation (13 per cent) The remaining 4 died in 17 to 19 hours after ligation A statistical comparison of these results, i e 30 per cent of 23 dogs as compared to 75 per cent of 24 dogs in the control group, using the chi square method and the Yates correction for small numbers, yielded a chi square of 7 4 and a P factor of less than 0 01

In comparison with the ergotamine tartrate series, it is apparent that DHE-45 was not only similar in its protecting action on the ventricular fibrillating mechanism, but also significantly increased the survival rate

Following the intravenous injection of DHE-45, electrocardiograms were obtained and compared with those taken immediately before giving the drug (Fig 5 on page 95) In almost every instance there was a slightly decreased sinus rate In over 50 per cent of records a slight increase in the P–R interval over the pre-drug record was apparent In the majority of records there was a small increase in the amplitude of the T waves

Immediately following ligation there was an elevation of the S–T segment in leads I and II, and this was accompanied by a fast sinus rhythm which persisted during the observation period (Fig 5) The rhythm was broken by bouts of rapidly forming ventricular extra-systoles, or, in many instances, by only an occasional ectopic beat, in three instances ectopic beats did not occur Within a half-hour the S–T segment had returned to, or was approaching, the pre-ligation base line

In the animals dying suddenly following occlusion, there were two instances in which a rapid sinus tachycardia was followed by ventricular tachycardia, ventricular fibrillation, and death within 12 minutes (Fig 5B) The appearance of ventricular tachycardia did not necessarily mean a fatal termination, for in one instance it was seen to appear in 3 minutes and lasted 25 minutes Tracings taken 24 hours following the ligation showed for the most part a sinus rhythm Ventricular extrasystoles were frequent, while T waves were inverted and increased in amplitude

In two instances a ventricular bigeminal rhythm was noted, in one this appeared shortly after ligation, and the animal died in ventricular fibrillation in 11 minutes The other was observed in the 24-hour record, and the animal survived the experiment A 2 1 A-V block occurred in 13 minutes after ligation in one animal, and S-A block was observed in the 24-hour record of another animal, both of which survived

DISCUSSION

In previous reports (Manning *et al* , 1939, and McEachern *et al* , 1940, 1941) it was suggested that a reflex mechanism that caused constriction of the non-occluded branches, resulting in a generalized ischæmia of the myocardium, may have been responsible for the onset of ventricular fibrillation and the high mortality that followed the occlusion It was suggested also that the mechanism might be associated with certain areas of myocardium more readily affected by the ischæmic process providing a source for ectopic beats progressing to fatal ventricular fibrillation

In view of our earlier studies, and the work of others, the prevention of this fatal rhythm seemed to resolve along two pathways First, by the use of antispasmodic and coronary dilator drugs, which may limit the area of ischæmia to the infarcted portion, and perhaps reduce the amount of non-functioning myocardium Secondly, by the use of sympathetic inhibiting agents in an attempt to reproduce the results obtained following cardiac sympathectomy (McEachern *et al* , 1940)

It has been shown that antispasmodic and coronary dilator drugs have some effect in reducing mortality following experimental coronary occlusion (McEachern *et al* , 1941, Le Roy *et al* , 1941, 1942, Gilbert 1942, and Gold *et al* , 1937) Their use in the treatment of coronary occlusion clinically has also been reported (Nathanson, 1936, Gold, 1939, Le Roy *et al*, 1941, Elek and Katz, 1942, Gilbert, 1942, Falk, 1942, Swanson, 1945, and Gerger, 1945) Consequently, it was anticipated that demerol might decrease the mortality In these experiments, however, 7 of the 12 dogs died within 4 minutes of the ligation and the remaining 5 survived the observation period In these 7 cases fatal ventricular fibrillation, recorded by the electrocardiogram, occurred in a shorter period (2 to 4 minutes) than that usually seen in

the control dogs (8 to 12 minutes)   Over half of the dogs were hyperexcitable and in general it appeared that the more excitable the animal the earlier was the onset of the ectopic rhythm

Since the pre-fibrillation ventricular rhythm (and fibrillation) occurred so rapidly following the occlusion, it would seem that demerol increased the excitability of the myocardium Demerol has been used by Gerger (1945) in acute myocardial infarction and by others for the relief of pain, particularly during labour (Hori and Gold, 1944 , and Flatt, 1946)   In the clinical reports on the use of demerol there appears to be no evidence of the exciting or stimulating effect seen in these experiments

In the experiments carried out with ergotamine tartrate and DHE-45 the " immediate " (i e within the first 15 minutes) mortality was considerably reduced, to 15 per cent and 13 per cent respectively, as compared with the control series mortality of 50 per cent in a similar time It was shown that this was due to the inhibition of fatal ventricular tachycardia and fibrillation In the ergotamine tartrate group, the mortality had increased to that seen in the control series by 19 hours after the occlusion , this we considered due to the combined effect of drug toxicity and infarction   In the DHE-45 experiments, however, the mortality remained low (30 per cent) approximating the results obtained in the cardio-sensory denervation experiments (10 per cent mortality), although pain did not appear to be influenced   Clinically, the DHE-45 experiments resembled the control experiments, except for the mortality rate which was significantly lower in the DHE series

In the cardiac sympathetic denervation experiments it was postulated that a possible reflex spasm, with the afferent side of the arc in the sympathetic and the efferent radicles in the vagus, was interrupted   An alternative view was that sympathetic denervation rendered the myocardium less susceptible to the onset of ventricular fibrillation (McEachern et al , 1940) Although the former hypothesis has received support (Le Roy et al , 1941, 1942, and Gilbert, 1942), it is difficult, in view of our recent results with DHE-45, to explain the reduction in mortality entirely on this basis, particularly in view of the more recent work on the nervous and reflex control of coronary blood flow (Katz and Joachim, 1939, 1945, and Gregg and Shipley, 1944 and 1946) which, at the present time, is by no means settled (Gregg, 1946)

DHE-45 acts on effector organs in such a way as to render them indifferent to sympathetic impulses (Rothlin and Brugger, 1945)   The drug is, therefore, not effective by interrupting the afferent side of such a reflex arc   If sympathetic efferent fibres carry constrictor impulses to the coronary arteries (Katz and Joachim, 1939), then it is still possible that coronary spasm (reflex or otherwise) may be a factor in the onset of fatal tachycardia and fibrillation following coronary occlusion

The exciting effects of adrenalin and sympathetic stimulation in producing fatal ectopic heart rhythms experimentally (Wiggers, 1930, Naham and Hoff, 1934, Hoff and Naham, 1935, Melville, 1946, and Philips et al , 1946) and the deleterious effects of sympathetic stimulation and adrenalin in coronary heart disease have been described by various writers (Nathanson, 1936, Eppinger and Levine, 1943, and Raab, 1943, 1944, 1945)   From the existing evidence it would appear that these effects are the result of a direct action on the heart rather than secondary to a decrease in coronary flow   A similar myocardial excitability follows sudden coronary occlusion and this can likewise be depressed or inhibited by removal of sympathetic nerves or by inhibition of the sympathetic effector mechanism with DHE-45 It would appear reasonable, therefore, to assume that a direct sympathetic excitor mechanism is an important factor in producing the fatal ectopic rhythm following sudden coronary occlusion   In the cardio-sensory denervation experiments both afferent and efferent fibres have been removed.   This may be effective through the abolition of reflex constrictor impulses to the coronary bed, or by the removal of the source of adrenalin, both locally in the heart (Hoffmann et al , 1945) and from the adrenals   In the DHE-45 experiments efferent endings only have been affected, pain was unaffected and it is expected that the amount of circulating

adrenalın is high but is rendered ineffective by the DHE-45 It has been shown (Hoff and Nahum, 1934) that removal of the stellate ganglia and adrenal glands prevents the occurrence of benzol- and electrically-induced ventricular fibrillation, but that if adrenalın is given to the animal fibrillation occurs Unfortunately, adrenalın was not given in the cardiac denervation experiments It is possible, however, that complete cardio-sensory denervation by the abolition of pain prevented the release of adrenalın from the adrenals (or possibly locally in the heart) which must occur with the sudden painful and distressing attack. In this connection it is interesting to note that in the sympathectomized series the 2 animals that did not survive the occlusion died in ventricular fibrillation, and both experienced some degree of pain, indicating that cardio-sensory denervation had not been complete

Furthermore, from the survival times during the 24-hour period (Table I) it appears, both in these studies and in the previous reports, that the "immediate" mortality (i e within the first 15 minutes) in the control group and in the animals treated with antispasmodic and coronary dilator drugs is of the same order During the remainder of the 24-hour period little or no further increase in mortality occurred in the treated group, whereas in the control group the mortality had increased to 75 per cent Antispasmodic and coronary dilator drugs, therefore, appeared to have no effect on this "initial" mortality (due to ventricular fibrillation) On the other hand, DHE-45 markedly decreased the early initial mortality (13 per cent), but later in the 24-hour period (18 hours) a small further increase of 18 per cent in mortality occurred

Although experimental findings in the dog cannot be applied directly to coronary artery occlusion in man, the similarity in clinical features is most striking There are a number of reports of ventricular fibrillation graphically recorded as the terminal event following sudden coronary occlusion in man (Hamilton and Robertson, 1933, Leary, 1935, Nathanson, 1936, Smith, 1939, Miller, 1939, Le Roy and Snider, 1941, Thompson, 1941, and Falk, 1942) Since most patients suffering a sudden coronary occlusion are not seen by the physician for some time, little is known about the frequency of cardiac irregularities immediately following the attack In patients who survive the immediate occlusion, frequent extrasystoles, ventricular tachycardia, and other cardiac irregularities that lead to ventricular fibrillation are not considered to be common, in all probability the earlier the patient is seen, the more frequently such irregularities will be observed Furthermore, when sudden death occurs in such cases some hours or days following the occlusion, a rapid and fatal ventricular tachycardia and fibrillation is responsible (see above) Consequently, if therapy that will inhibit the development of a rapid ectopic rhythm can be instituted early, there may be a reasonable hope of reducing the immediate mortality of sudden coronary occlusion Experimental and clinical studies suggest that such treatment may be further enhanced by the early use of coronary antispasmodic and dilator drugs, presumably through the favourable effects on coronary circulation

SUMMARY AND CONCLUSIONS

Sudden occlusion of the left circumflex branch of the left coronary artery in conscious dogs, resulted in fatal ventricular fibrillation in 75 per cent of 24 animals within the first 24 hours (50 per cent within first 15 minutes) Previous studies (McEachern et al, 1940) have shown that this mortality can be reduced to 10 per cent, or less, if bilateral cardiac sympathectomy is carried out prior to the ligation

Demerol was not effective in reducing the initial mortality and ventricular fibrillation occurred rapidly in all fatal cases (58 per cent of 12 animals) The 24-hour mortality, however, did not increase further during the 24-hour period Animals that recovered did so in spite of a rapid ventricular tachycardia although this was invariably followed by fatal ventricular fibrillation when it occurred in the control series

Ergotamine tartrate prevented the occurrence of post-ligation ventricular tachycardia and

fibrillation in 12 out of 13 dogs Toxic manifestations were observed in all cases, both clinically and cardiographically, with the result that although survival time was increased the 24-hour mortality rate was unchanged (70 per cent) from that seen in the control group

Dihydro-ergotamine prevented the occurrence of post-ligation ventricular tachycardia and fibrillation in 20 of 23 experiments The toxic manifestations seen in the ergotamine tartrate group did not occur In this group the "immediate" or initial mortality (i e, within 15 minutes) was 13 per cent and the 24-hour mortality 30 per cent It is considered that the drug was effective by inhibiting, through its action on the sympathetic efferents, the ventricular tachycardia and fibrillation that result from sudden coronary occlusion

A discussion of these results, together with other reports on the effect of sympathetic inhibiting agents and coronary antispasmodic and vasodilator drugs in preventing sudden death following acute coronary occlusion is presented

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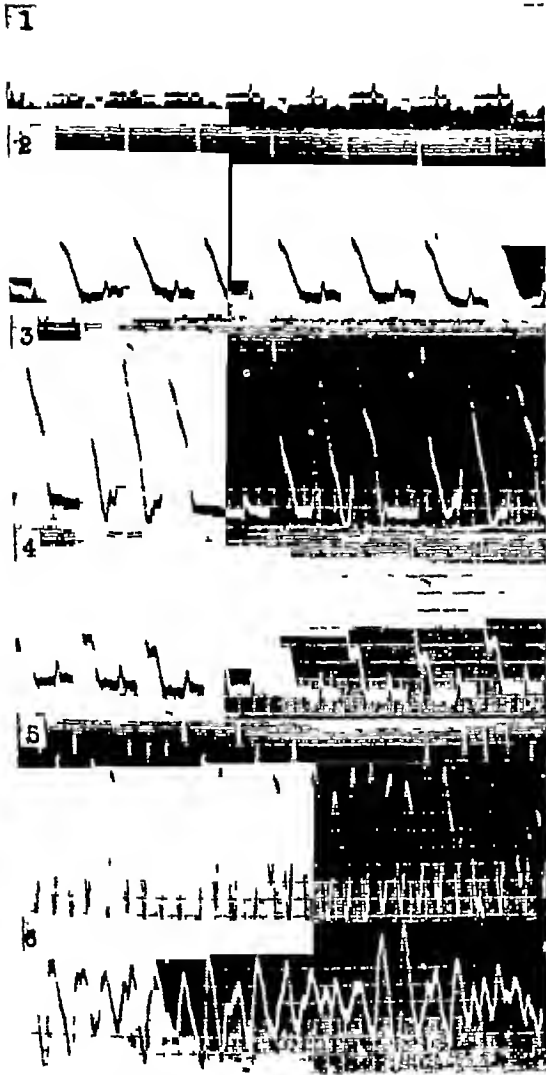
FIG 1 —Electrocardiograms, lead II, showing typical changes following sudden ligation of the circumflex branch of left coronary artery of the conscious dog (control series) Fatal ventricular fibrillation (D 3/46)
(1) Before ligation (2) Three minutes after ligation (3) Five minutes after (4) Eleven minutes after (5) Twelve minutes after (6) Thirteen minutes after ligation

FIG 2 —Electrocardiograms, lead II, showing typical changes following sudden ligation of the circumflex branch of the left coronary artery of dogs given demerol prior to the occlusion survival type series of records Note rapid ventricular tachycardia not followed by ventricular fibrillation, a feature occurring in this group only (D 19/46)
(1) Before ligation (2) Immediately after ligation (3) Two minutes after (4) Five minutes after (5) Twenty minutes after (6) Twenty-four hours after ligation

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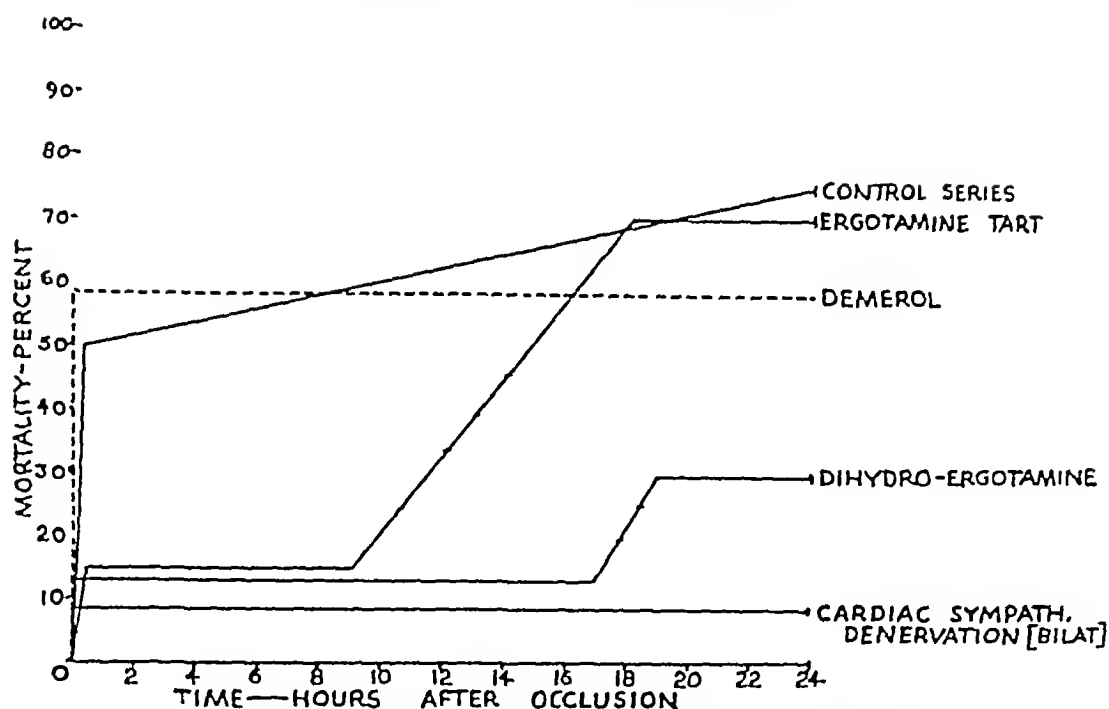
FIG 3 —Survival times and mortality rates during the 24-hour period following sudden ligation of the circumflex branch of the left coronary artery
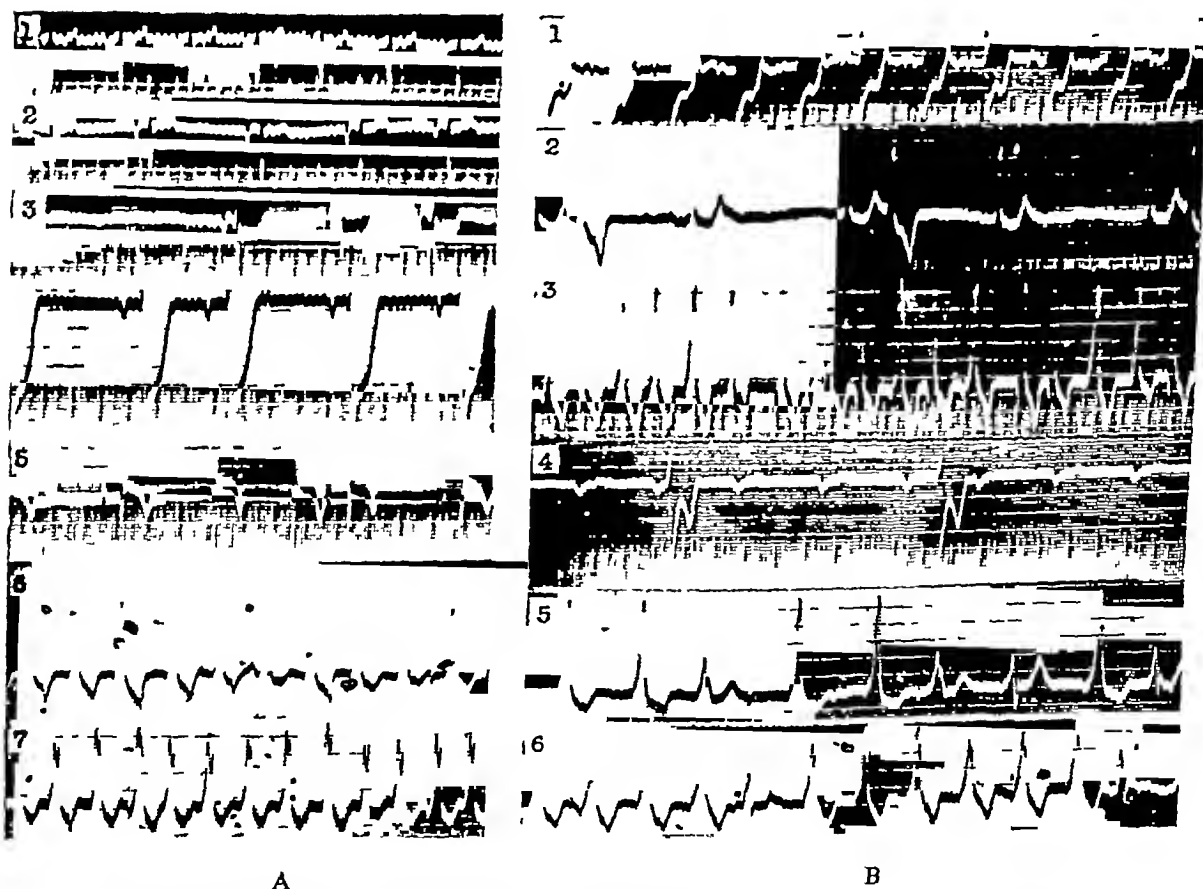
A   B

FIG 4 —Electrocardiograms, lead II, following sudden ligation of the circumflex branch of the left coronary artery of dogs given ergotamine tartrate prior to the occlusion

(A) Survival type series of records   (D 32/46)
    (1) Before ergotamine   (2) After ergotamine and before ligation   (3) One and a half minutes after ligation   (4) Twelve minutes after   (5) Eight hours after   (6) Seventeen hours after   (7) Twenty-four hours after ligation

(B) Electrocardiograms from several different dogs showing the various abnormalities that occurred in the ergotamine treated group
    (1) D 28, twenty-five minutes after ligation   (2) D 38, eight-and-a-half hours after ligation   (3) D 33, twelve hours after ligation   (4) D 26, thirty minutes after ligation   (5) D 39, fifteen hours after ligation   (6) D 27, five-and-a-half hours after ligation
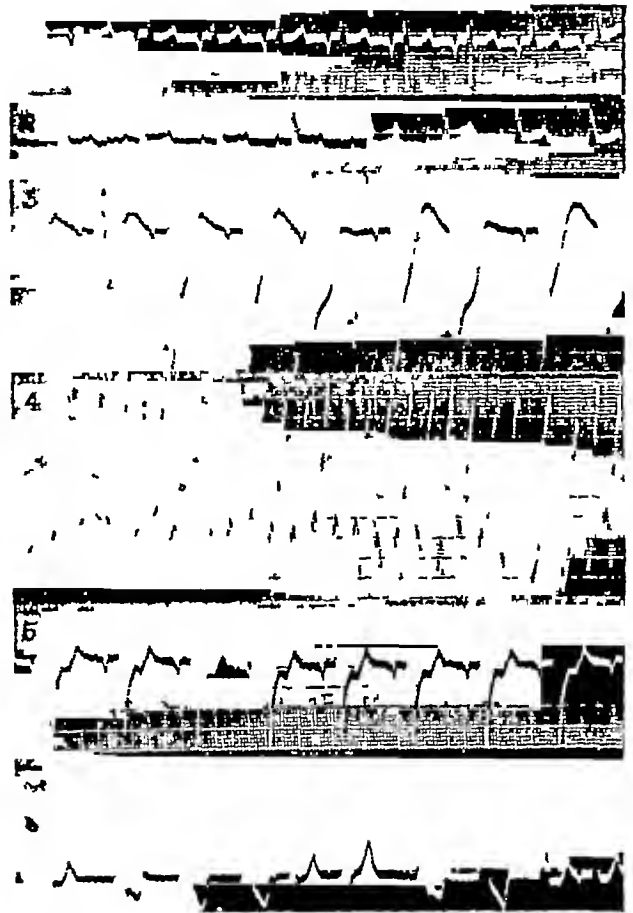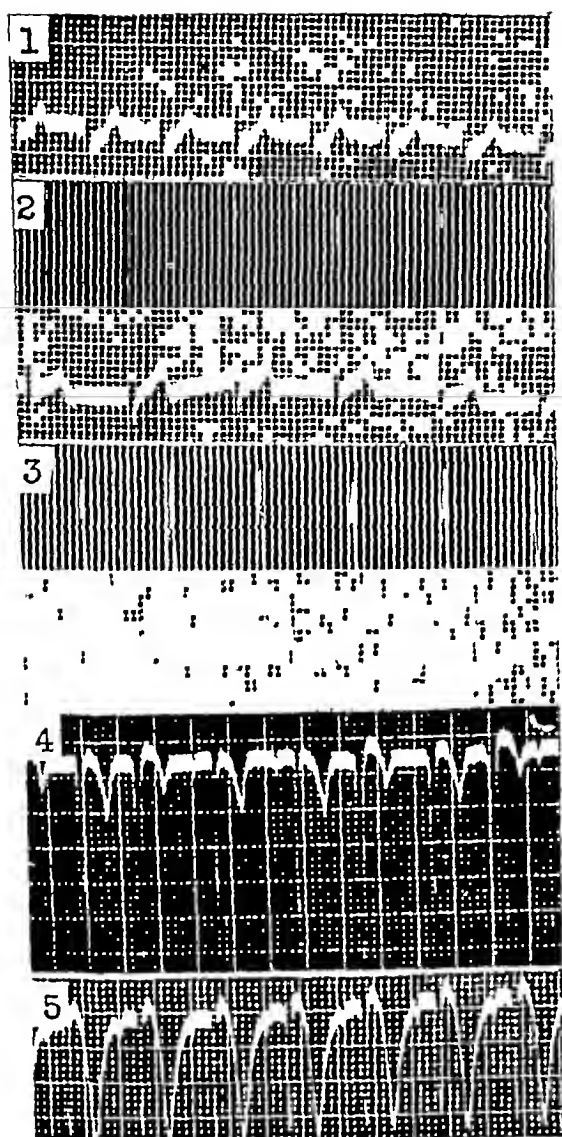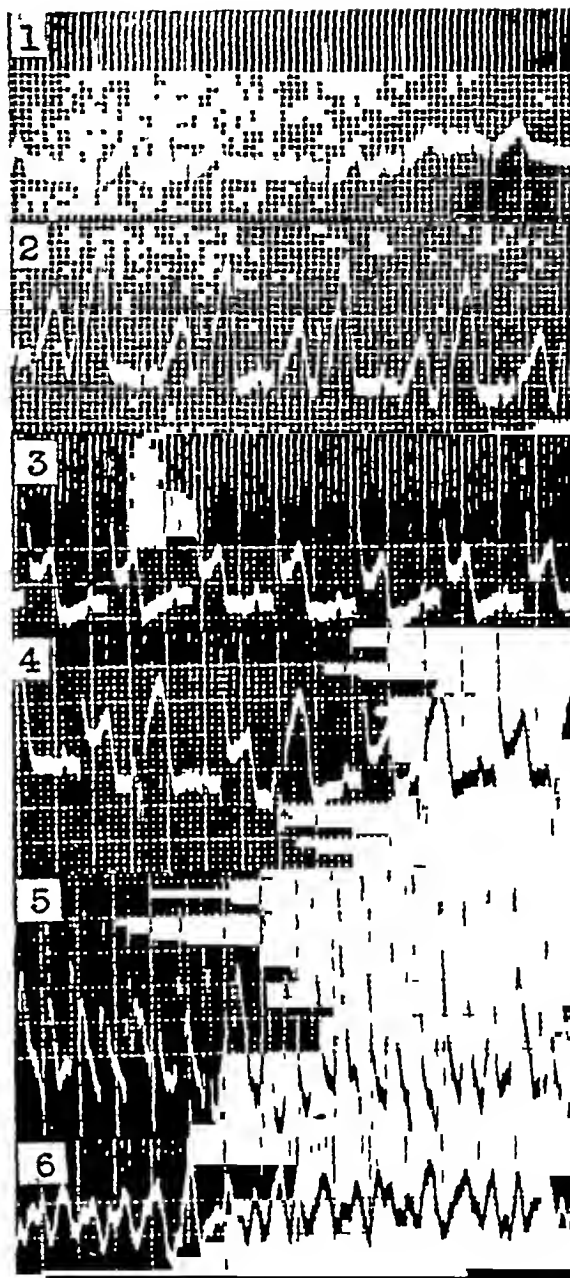
FIG 5.—Electrocardiograms, lead II, following sudden ligation of the circumflex branch of the left coronary artery of dogs given dihydro-ergotamine prior to the occlusion
(A) Survival type series of records   (D 63/46)
    (1) Before DHE-45   (2) After drug and before ligation   (3) Two-and-a-half minutes after ligation   (4) Twenty-four hours after ligation   (5) Three days after ligation
(B) Fatal type series of records   (D 47/46)
    (1) Before ligation   (2) Thirty seconds after ligation   (3) One-and-a-half minutes after   (4) Three-and-a-half minutes after   (5) Five minutes after   (6) Six minutes after ligation.

UNUSUAL LONGEVITY IN ANEURYSM OF THE THORACIC AORTA

BY

RALPH KAUNTZE

From St George's Hospital

A healthy looking man, aged 36, complaining of recurrent streaking of the sputum with blood and of difficulty in swallowing solids during the previous month was admitted to St George's Hospital under the care of Dr F Golla in 1921 In addition, there had been pains in the back of the head and left side of the neck, which had worried him on occasion since 1919, latterly numbness of the left arm had been noted

From 1900 to 1919 he had served in the regular Army, contracting enteric and malaria in 1901 while in South Africa Since 1919 he had been employed as a carman, a not exceptionally strenuous occupation He had one son alive and well, and his wife had had no miscarriages

Examination at this time revealed visible pulsation above the manubrium sterni, a tracheal tug, and pulse inequality the left radial being variable in volume but always weaker than the right The apex beat was four and a half inches from the mid-line in the fifth left interspace, there was a ringing aortic second sound and an aortic systolic murmur conducted upwards, the systolic blood pressure in the right arm was 132 mm (that in the left arm was later recorded as 80 compared with 112 in the right arm) There was a systolic murmur over the lower cervical spines and dullness at both lung apices in front, and inequality of the pupils

The blood Wassermann reaction was positive The date of primary infection is not known, although his earlier notes give 1900, this is now denied by the patient with some vehemence

A radiograph with screening was reported as showing a sacculated mass to the left of the aorta in which pulsation was seen, thereby confirming a clinical diagnosis of aortic aneurysm During this period in hospital his general condition continued poor, the sputum was repeatedly blood-tinged, and at times there was orthopnœa

From September to December 1921 he received potassium iodide orally and mercury by inunction In December 0 35 g of novarsenobenzol was given intravenously, and in the succeeding four weeks a further 2 5 g His condition at discharge, on January 21, 1922, was noted as " little changed," the sputum being intermittently tinged with blood and the neck pain persisting

During the subsequent eight months he was confined to bed, after which he slowly started to get about, the sputum being no longer blood-stained Although he did not attempt any regular work, he remained reasonably well until September 1931 when he again attended St George's Hospital complaining of giddiness and pains in the chest There had not been further anti-syphilitic treatment since 1922

In July 1932 after two short courses of sulphostab and bismuth injections the blood Wassermann reaction was negative Bismuth injections and mercury by mouth were given at intervals up to 1940, when the blood Wassermann reaction was again negative and the Kahn reaction

positive   Meanwhile, in 1933, he successfully recovered from an operation for acute appendicitis, and in 1934 from an attack of jaundice, at this latter occasion a radiograph showed " a saccular aneurysm with calcification "

In 1941 there were again small hæmoptyses throughout the year   The aneurysm increased in size between 1940 and 1942, when a swelling was noted between the top of the manubrium and the angle of Louis   In April 1944 there was sudden onset of aphasia, possibly embolic in origin, from which recovery has not been complete

In May 1946 he was admitted to St George's Hospital under the care of Dr C B Levick, after a sudden increase in the size of the aneurysm, during the previous three weeks there had been weakness of the right arm and forearm, of gradual onset   Occipital and cervical pains were still at times troublesome   The initial symptom, and one that has been present intermittently throughout, was pain in the neck and occiput   The significance of this referred pain in the diagnosis of aneurysm of the aortic arch was emphasized by Graham Steell (1911)

Examination showed slight cyanosis of the lips, a pulsatile swelling four inches transversely

FIG 1 —X ray of the aneurysm with calcification in the aorta   May 1946

by three and a half inches longitudinally occupying the whole area of the manubrium, with a weaker and more expansile area in the right periphery, there was no discoloration of the overlying skin

The pulse was collapsing in type, rate 65–70, the left radial pulse being weaker and lagging behind the right, the pulse inequality being little altered by forced inspiration or expiration There was dullness from below the right clavicle to the fifth rib extending two inches to the right of the sternum, the apex beat was four inches out in the fifth left interspace, and there were soft aortic systolic and diastolic murmurs   B P right arm 175/70, left 155/65

FIG 2 —Lateral and anterior views of he aneurysm presenting through the manubrium   May 1946

There were motor aphasia, moderate weakness of all movements of right arm and forearm particularly noticeable in skilled actions, slight wasting of these muscles, hypoalgesia over a small area of the flexor surface of the right forearm, but no positional loss   The abdominal reflexes were absent, the tendon reflexes equal except for ankle jerks which were not elicited, the plantar responses flexor, and the pupils regular, equal, and reacting   There was moderate arteriosclerosis of the retinal vessels and left vitreous opacities   The vocal cords showed normal movements   The weakness of the right arm seemed probably the result of a cortical thrombosis

X-ray examination showed an aneurysm of the aortic arch, with calcified plaques in the aorta and in parts of the aneurysmal sac, left ventricular hypertrophy, trachea displaced to the right, left diaphragm raised, ? phrenic palsy   By May 15, 1946, a small increase in the size of the visible portion of the aneurysm had occurred, since when there has been little change and equilibrium appears to have been restored   The occipital and neck pains are not now evident, there is no dysphagia, and there is little complaint

DISCUSSION

The first symptoms referable to the aneurysm occurred in 1919, and in 1921 the lesion was sufficiently advanced to cause dysphagia and hæmoptysis, so that the probable duration in this aneurysm is not less than 27 years   Colt (1926) from a consideration of 482 cases of saccular aneurysm of the thoracic aorta in men found the average duration of life from the onset of symptoms 19 months, among 72 women the duration was 22 months   The expectation of life in aneurysm of the ascending or transverse aorta amongst men with onset at 60 years was rather less than twice that with onset at 35 years   whereas expectation with aneurysm of the descending aorta was the reverse of this

De Havilland Hall (1913) in 27 private cases gives the duration after diagnosis as 32 months, and suggests that three years represents the average expectation from first symptom, he also mentions an instance of survival for 15 years in a builder's foreman

Herz (1919) noted a patient, aged 57, with aneurysm of the ascending aorta of 16 years' duration, still alive at the time of the report   Stewart and Garland (1932) record a patient with saccular aneurysm of the aortic arch, first diagnosed at the age of 33, who lived for a further 29 years during which he enjoyed good health, working as a janitor, eventually death resulted from a hypernephroma   he had received iodides for two months and then no further treatment

SUMMARY

A case of aneurysm of the thoracic aorta of prolonged duration is recorded

In 1921 the aneurysm was " weeping," but by the end of 1922 the patient was fairly well   Hæmoptysis, after being present in 1921, recurred temporarily in 1934 and again in 1941

In 1921 treatment consisted of mercury inunctions, potassium iodide, and later five injections of novarsenobenzol, following which there was no further anti-syphilitic treatment until September 1931

In 1946 his condition is still reasonably good

I wish to thank Dr C B Levick for permission to publish this case

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COARCTATION OF THE AORTA   II. CLINICAL FEATURES

BY

CRIGHTON BRAMWELL

From the Department of Cardiology, University of Manchester

This paper is concerned with the clinical features of coarctation of the aorta, and is based on a group of 26 cases observed by the author and described in the St Cyres' Lecture, delivered on June 6, 1945   A paper on the collateral circulation in coarctation of the aorta has been published (Bramwell and Jones, 1941), and a further paper on the radiological diagnosis of the condition will follow   all three are based on the same series of cases

Coarctation of the aorta has long been familiar to anatomists, but until comparatively recently it generally eluded the clinician   In 1928 Maude Abbott was able to collect from the literature 200 cases over three years of age that had come to autopsy, but, of these, only 21 had been diagnosed during life as coarctation and 7 others as obstruction of the aorta   The same year Roesler published his classical paper on the radiological diagnosis of coarctation, and the following year Railsback and Dock published similar observations   Fray added a further paper in 1930

These radiological observations provided the Mulberry Harbour that enabled clinicians to invade a territory hitherto dominated by morbid anatomists   Many cases have since been reported and I myself have seen 26* in the last fifteen years, 11 in private practice, 8 at my outpatient clinic at the Manchester Royal Infirmary, and 7 in recruits referred to me by medical boards of the Ministry of Labour and National Service during the war

Autopsy statistics suggest that the incidence of this condition is about one per thousand Fawcett (1905) found 18 cases in 22,316 autopsies at Guy's Hospital, an incidence of 0 08 per cent, and Evans (1933) 26 cases in 19,217 autopsies at the London Hospital, an incidence of 0 14 per cent, but I am inclined to think that the condition may be more common than these figures suggest, for I have reason to believe that coarctation sometimes escapes detection even at autopsy

CLASSIFICATION

Most authors have followed Bonnet's (1903) classification and have described two types, the " infantile " and the " adult "   In the former, which may be regarded as a persistence or exaggeration of the anatomical relations that exist before birth, there is a diffuse narrowing of the aortic isthmus   In the latter the narrowing, which is in the immediate vicinity of the insertion of the ductus arteriosus, may be so abrupt as to suggest that the aorta had been constricted by a ligature   The adult type was attributed by Craigie (1841) and some subsequent workers to an extension of the normal process that leads to occlusion of the ductus arteriosus after birth   This hypothesis is attractive, but there is considerable evidence in support of the view that the adult form also is due to an error in development at the junction of the primitive fourth and sixth branchial arches, an error that Maude Abbott suggests does not produce its effect till after birth when kinking of the descending limb of the aortic arch results from traction by the obliterated ductus

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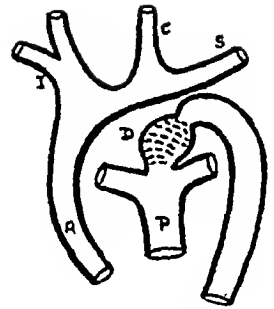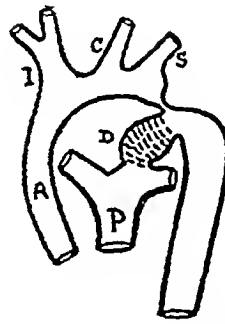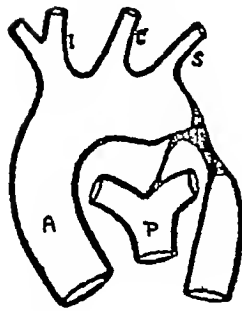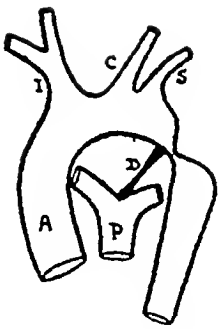* Five more cases seen since May 1945 will be reported later

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FIG 1 —Coarctation Evans's Types 2 and 3   FIG 2 —Coarctation Evans's Types 1 and 4
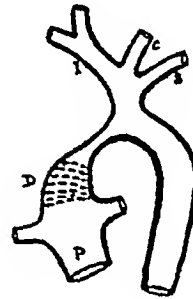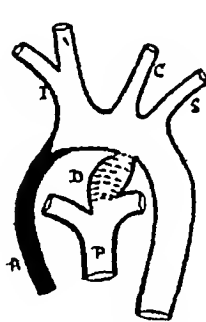

FIG 3 —Coarctation Evans's Types 5 and 6

This classification, though useful, is not entirely satisfactory, and William Evans (1933) suggested an alternative classification based on purely topographical considerations He described six anatomical varieties of coarctation of the aorta   I would suggest that Evans's classification might, without detriment, be simplified by dividing his six types into three groups In Group I (Fig 1), I would place Evans's Types 2 and 3 in both of which the ductus is closed and the proximal portion of the aorta is hyperplastic   Type 3 differs from Type 2 in that the coarctation is complete with atresia of the distal portion of the aortic arch, whereas in Type 2 there is merely a stenosis this is a difference of degree rather than of kind   Similarly Group II (Fig 2) would include Evans's Types 1 and 4, in both of which the ductus is patent and the proximal portion of the aorta is hypoplastic   These two types are essentially similar but differ from one another in that in Type 4 the interruption between the arch and descending aorta is complete, whereas in Type 1 there is a narrow communicating channel between them, again a difference of degree   Hypoplasia is rare compared with hyperplasia of the aorta and was present in only 10 per cent of Maude Abbott's cases   Lastly I would place Evans's Types 5 and 6 together in Group III (Fig 3), since in both the only communicating channel between heart and aorta is the patent ductus   Admittedly there is an important developmental difference between these two types   in Type 5 the proximal portion of the arch is merely atresic or occluded, whereas in Type 6 it is absent

The expectation of life (Table I) in these three groups is very different   In the first, in which the ductus is closed and the proximal aorta hyperplastic, 7 of Evans's 11 cases reached maturity, of 11 cases in the second group, in which the ductus is patent and the proximal aorta hypoplastic, 1 died in childhood and only 1 reached adult life, while in the third group none of the 6 cases survived infancy   The relatively favourable prognosis in Group I as compared with Groups II and III is probably, in part at any rate, attributable to the fact that the " infantile " type of coarctation is often associated with other grave errors of development, whereas in the so-called " adult " type of coarctation, in which there is an extreme degree of

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TABLE I

PROGNOSIS OF EVANS'S SERIES

Group	Type (Evans)	Ductus	Proximal aorta	Correlation	Age at death			Total
					Infant	Child	Adult	
I	{ 2 3	Occluded Occluded	Hyperplastic Hyperplastic	Partial } Complete }	1	3	7	11
II	{ 1 4	Patent Patent	Hypoplastic Hypoplastic	Partial } Complete }	9	1	1	11
III	{ 5 6	Patent Patent	Occluded Absent		6	0	0	6
					16	4	8	28

stenosis, this is not the case. Maude Abbott found that of 82 cases in which death occurred within the first year, in 50 (61 per cent) the coarctation was associated with some other major congenital anomaly such as bilocular or trilocular heart, transposition of the arterial trunks, or pulmonary atresia, whereas in 155 cases in which life was prolonged beyond one year an associated major anomaly was present in only 13 (8 per cent) and, in these 13, coarctation was either so slight as to be of no importance or of the infantile type. In the older group, however, other minor congenital defects such as bicuspid aortic valve, subaortic stenosis, or abnormal origin of the vessels arising from the arch of the aorta were common and occurred in 57 of the 155 cases.

Clinically, we may divide cases of coarctation into two groups in accordance with whether the ductus is closed or patent. In patients who survive infancy the former is much the more common. In Abbott's series of 200 cases the ductus was patent in only 18 and in my 26 in 3 or possibly 4 cases. *The state of the ductus is important*, since a patent ductus provides for the passage of blood from heart to aorta beyond the coarctation and thereby eliminates the necessity for a collateral circulation. Consequently, in such cases, there may be no pulsating vessels on the back or front of the chest and no notching of the ribs. This renders diagnosis more difficult. When the ductus is patent the upper part of the body is supplied by the branches of the aortic arch arising above the coarctation, while the trunk and lower limbs are supplied chiefly by blood entering the descending aorta through the ductus.

CLINICAL MATERIAL

Age. In Table II, I have arranged my cases in accordance with the age at which they first came under observation and have indicated their condition in May 1945. 13 were then alive, 10 had died, and 3 had been lost sight of. These figures are summarized in Table III.

Three of my patients were children, 3 were over 40 years of age, and the remaining 20 were between the ages of 18 and 37 at the time they were first seen. The small number of children in my series is due to the fact that both in hospital and in private practice the great majority of my patients are adults.

Sex. In Abbott's series of 200 cases, one-quarter were females and three-quarters males. If we exclude the 9 " Service cases," drawn from a special section of the population, almost entirely male, the ratio of the sexes in the remainder of my series is 6 11. Why the condition should be so much more common in the male sex it is difficult to say unless it be that, in reality, the sex incidence is equal, but, since women lead a more sheltered life, they are less exposed to the physical strains so often responsible for the development of heart failure in males.

TABLE II
BRAMWELL'S SERIES

Case No	Sex	Age first seen	After history 1945	
			Age living	Age at death
1	M	9	—	11
2	M	11	—	23
18	M	11	—	12
16	M	18	21	—
20*	M	18	20*	—
22	M	18	19	—
25	M	19	19	—
15	M	20	—	23
14	M	21	25	—
11	M	23	lost sight of	—
24	F	23	—	23
13*	M	24	29*	—
8	F	25	—	27
21	M	26	lost sight of	—
12	M	27	lost sight of	—
23	M	27	28	—
17	M	30	38	—
7	M	31	45	—
4	M	31	39	—
9	F	31	—	36
10	F	32	39	—
19	M	32	35	—
26	F	37	37	—
5	M	46	—	52
3	F	51	—	52
6	M	58	—	62

*See p 125

TABLE III
AGE AND PROGNOSIS OF BRAMWELL'S SERIES

Ages in 1945 or at death	Living	Dead	Untraced	Total
10–19	2	2	—	4
20–29	5	4	3	12
30–39	5	1	—	6
40–49	1	—	—	1
50–59	—	2	—	2
60–69	—	1	—	1
Totals	13	10	3	26

This would render it more likely for the condition to remain latent in the female and to pass unnoticed unless it were discovered accidentally in the course of some routine examination. This hypothesis, however, would not account for the high incidence of males in Abbott's series in which the figures are based on autopsy statistics, but for the fact that autopsies are performed less often in the female than in the male   Dr W Susman (1946) informs me that in a consecutive series of 2000 autopsies performed at the Manchester Royal Infirmary 63 per cent were males and only 37 per cent females

1*

Service Cases Nine of the young adults must be placed in rather a different category from the others since they would not have come under observation but for the war The lesion in these men was discovered in the course of a routine examination and most of them had been unaware of any disability and had no cause to seek medical advice Seven were recruits referred to me by recruiting medical boards, one (Case 25) consulted me privately having been rejected for service, and one (Case 21) was a serving soldier referred to my clinic

TABLE IV
DETAILS OF "SERVICE CASES"

Case	Age	Symptoms	Athletic	Remarks
14	21	Dysp 2-3 years	till 19	
11	23	—	+ at school	
15	20	Septicemia	—	Aortic incompetence
16	18	Dysp and pain 2 years	at school	
19	32	—	Heavy work	Dyer
20	18	—	++	Swim, rugger, cycle, climb
21	26	Epistaxis	—	Serving soldier
22	18	—	Heavy work	Patent ductus
25	19	—	+	

Six of these men were free from symptoms and had been unaware of any disability prior to the discovery of their cardiac lesion at the medical board Of the other three, one (Case 14), aged 21, had played football up to the age of 19, but subsequently complained of tiredness and some breathlessness on exertion another (Case 16), a lad of 18, had complained of dyspnœa and pain in the calves for two years but had played games at school The third (Case 21) had been known to have heart trouble from childhood, and had always avoided strenuous exertion since it was liable to cause epistaxis

TABLE V
PERLMAN'S SERIES OF AMERICAN ARMY RECRUITS

Case	Age	Heart disease diagnosed	Athletic
1	28	—	+
2	21	—	+
3	21	—	?
4	19	—	?
5	22	14	++
6	21	early childhood	0
7	20	—	+
8	20	11	0
9	18	—	++
10	23	8	+
11	32	22	++
12	25	early childhood	0
13	18	—	+

It is interesting to compare this group with the series reported by Perlman (1944) from American Army recruits. The ages of the two groups are very similar, 10 of Perlman's cases and 7 of mine being under 25 and none over 33 Seven of Perlman's cases and 6 of mine had no knowledge of heart disease and were free from symptoms, 8 in each series had participated actively in athletics or had been employed in laborious physical work One of my patients (Case 20) was a good athlete and had gone in for swimming and played Rugby football at the

Manchester Grammar School he also was a keen cyclist and climbed in Switzerland One in Perlman's series played semi-professional basket-ball

SYMPTOMS

The age at which patients first come under observation is a matter of chance, since some seek medical advice for symptoms attributable to their coarctation, others for symptoms due to some intercurrent disease, and in others, unaware of any disability, the lesion is discovered accidentally in the course of a routine examination The age at which symptoms first appear however, does seem to be of significance in prognosis and I have accordingly classified my cases in three groups

1 In 5 symptoms dated from childhood Of these, 2 died in the second decade, 2 in the third, and 1 has been lost sight of

2 In 11 patients symptoms first appeared between the ages of 16 and 57 Four of these are still alive aged 21, 25, 29, and 37 respectively, 1 has been lost sight of, and the other 6 are dead

• 3 Of the remaining 10 patients 1 has been lost sight of and, up to May 1945, the other 9 were either free from symptoms or complained only of symptoms due to some disease unconnected with their coarctation Their age incidence was from 19 to 45

CASES IN WHICH SYMPTOMS DATED FROM CHILDHOOD

Case 1 A boy, aged 11, was referred to me in December 1934 by Dr John Ward from the Royal Manchester Children's Hospital to which he had been admitted with a sore throat Prior to severe epistaxis at the age of 9 he had been free from symptoms In addition to coarctation, he had subaortic stenosis with great cardiac enlargement (see p 112) He was readmitted to hospital in May 1936 with acute pericarditis with effusion following a further attack of tonsillitis From this he made a good recovery, but a few months later developed congestive heart failure from which he died

Case 8 A woman of 25 consulted me regarding her fitness for pregnancy Her chief complaint was pain in the back Two years later she developed subarachnoid hæmorrhage from which she died (see p 106)

Case 18 This boy appeared to be not only healthy but robust until, at the age of 11, he developed subacute infective endocarditis from which he died There was evidence, both clinical and radiological, of a patent ductus (see p 115)

Case 21 A serving soldier was referred to my clinic by Major Olav Kerr, R A M C Since childhood he had always avoided strenuous exertion since it was liable to produce epistaxis After three years' service as a draughtsman he decided to take a sapper's course for promotion, but this proved too strenuous for him and provoked dyspnœa Shortly afterwards he was invalided out of the service following pneumonia and has since been lost sight of

Case 24 (see p 113) A woman of 23 had been short of breath as long as she could remember and cyanosed in cold weather While in hospital she had two peculiar attacks in which she complained of paræsthesia in the lower limbs associated with a feeling of constriction in the lower sternal region Following her second attack she developed œdema and died of congestive heart failure In this case the presence of a widely patent ductus (Fig 6) was confirmed post-mortem and the coarctation was of the infantile type

CASES IN WHICH SYMPTOMS DEVELOPED LATER IN LIFE

Case 2 A boy of 11 was referred to me in 1930 on account of palpitation following a minor gastro-intestinal disturbance and was found to have coarctation of the aorta Throughout his time at the Manchester Grammar School he had no illness, and played cricket and swam He remained free from symptoms till 1942 when he developed subacute infective endocarditis from which he died

Case 3 A woman aged 51 first noticed tightness in the chest and palpitation at the age of 50 She had worked hard all her life and had never required medical attention previously, but had always preferred a standing job as she got pain in the left chest if she had to sit for long (see p 107)

Case 5 (see p 107) A man, aged 46, was referred to me complaining of a pain in the right arm of twelve months' duration When seen again four years later the pain had ceased to trouble him and he died of carcinoma of the stomach at the age of 52

Case 6 (see p 112) In March 1933, I was consulted by a man of 58 who had enjoyed good health and led an active life until twelve months previously, when he began to suffer from dyspnœa on exertion with a sensation of constriction in the chest Six months later he developed auricular fibrillation and shortly afterwards had a severe coronary occlusion In June 1935 he was still fibrillating but free from symptoms and able to carry on his business He died of lobar pneumonia at the age of 62 This man's freedom from symptoms was remarkable as, in addition to his coarctation, he had aortic incompetence and his heart was greatly enlarged Two years before death he underwent a major operation from which he made an excellent recovery

Case 9 (see p 122) A woman, aged 31, first noticed shortness of breath in the fourth month of pregnancy She was successfully delivered by Cæsarean section Two years later she again became pregnant and developed auricular fibrillation She died from congestive heart failure at the age of 36

Case 12 A varnish maker, aged 27, was referred to me by my colleague, Dr A Hillyard Holmes, whom he consulted on account of tiredness and attacks of vomiting a month previously Only since this attack had he been short of breath and suffered from palpitation This case has been lost sight of (see p 107)

Case 13 A storekeeper, aged 24, was referred to me on account of high blood pressure He had suffered from epistaxis since the age of 13, but had played football regularly until a year before I saw him, in spite of the fact that since 17 he had complained of pain in the back which troubled him intermittently As this man's only symptom prior to the age of 17 was epistaxis, and since he had participated actively in athletics up to the age of 23, I have not included him in the group of cases in which symptoms dated from childhood (see p 107 and 125)

Case 14 A leather worker, aged 21, who had been short of breath and easily tired for 2 or 3 years, prior to which he had been perfectly well and played football, was referred to me by a recruiting medical board in 1940 In May 1945 he was feeling fit and still anxious to join the Navy In this case it is very doubtful whether the temporary asthenia in 1938–40 was attributable to his coarctation

Case 15 A shop assistant, aged 22, was referred to me by a medical board in April 1941 He had always enjoyed excellent health and gone in for football, cricket, rowing, and cycling He was admitted to Crumpsall Hospital in March 1944 and I am indebted to the Superintendent, Dr Ramsay, and to Dr R W Luxton, for particulars of his illness at that time Blood culture on two occasions yielded *Staphylococcus aureus* and he was considered to be suffering from septicæmia He died five days later, but unfortunately permission for a necropsy was not obtained This young man never had any symptoms until ten days before his death His coarctation was unsuspected at the time of his acute fatal illness, which may have been acute infective endocarditis

Case 16 An accountant's clerk, aged 18, who had played tennis and cricket at school, began to complain of breathlessness and pain in the calves on exertion at the age of 17 He was referred to me by a medical board in January 1942 In May 1945 he informed me that though he had occasionally complained of tiredness he had not been off work

Case 26 A woman, aged 37, complained of slight dyspnœa on exertion, but otherwise, apart from an illness 17 years previously, had been free from symptoms excepting during her two pregnancies (see p 121)

DISCUSSION OF SYMPTOMS

To summarize these findings, the symptoms of which my patients chiefly complained were as follows

Three (Cases 2, 15, and 18) were free from symptoms until they developed infective endocarditis or septicæmia, three (Cases 1, 13, and 21) complained of repeated epistaxis, and one (Case 8) of migraine dating from childhood, it is interesting to note that she died of subarachnoid hæmorrhage Breathlessness and palpitation on exertion were common symptoms as was undue tiredness Eight of my patients complained of pain which affected various parts of the body This symptom merits more detailed consideration

Case 8 A parson's wife, aged 25, consulted me in July 1938 regarding her fitness for pregnancy In childhood she suffered from migraine and at school she was never able to play games because of

dyspnœa and palpitation   From 17 until her marriage at 24 she worked in an office and was never absent owing to illness except for occasional sore throats   When I saw her she was able to do all her housework with the help of a woman on one half-day a week, but complained of pain below the angle of the left scapula aggravated by exertion and occasional dyspnœa and palpitation   Apart from the pain in the back, she remained fairly well until 1940, when she had a subarachnoid hæmorrhage from which she died   The post-mortem findings in this case have been fully reported (Bramwell and Jones, 1941)

Abbott (1928) has called attention to the high incidence of subarachnoid hæmorrhage from rupture of a congenital cerebral aneurysm in patients with coarctation of the aorta

Pain was the presenting symptom in four other cases in this series

Case 3   The oldest woman in my series, first seen at the age of 51, had worked hard all her life and had been free from symptoms until twelve months previously, but since childhood if she sat for long, especially when leaning forward sewing, she got a pain in the left sub-mammary region, and for this reason she said she had always chosen a " standing-up job "   It is difficult to explain the association of the pain with the sitting posture in this case   From the age of 14 to 35 she worked as a weaver and after that as a maker-up in a warehouse   This employment involved lifting heavy packages   Three years before I saw her, the warehouse closed down, and since then she had been doing housework and taking a child to school each day   She had never required medical attention except for colds until she developed lichen planus at the age of 50   She then began to complain of tightness in the chest and pain similar to that which she had experienced when sitting for long   At that time she had venous engorgement in the neck but no œdema   A few months later she developed congestive heart failure from which she died

Case 5   A medical practitioner, aged 46, was referred to me in January 1934 by my colleague, Dr. Fergus R Ferguson, whom he had consulted the previous November for an aching pain of twelve months' duration, felt in the region of the insertion of the right deltoid, the outer side of the forearm, midway between the wrist and elbow, and in the tips of the fingers   It occurred at any time of the day or night, but was aggravated by using the arm driving his car which had a right-hand gear change   For twelve years he had been subject to cramp in the right arm and for five years his handwriting had been somewhat shaky   Having had chorea at the age of 14, he had been stopped playing games at school on account of his heart, but later played tennis   Following influenza in 1923 he had suffered from asthma until 1930   I obtained no history of other illness   His biceps and supinator jerks were diminished on the right side, but the triceps jerk was normal   On a neurological basis, Dr Ferguson considered that the signs and symptoms could only be accounted for by the somewhat unsatisfactory diagnosis of " brachial neuritis " and he was inclined to think that pressure from the dilated arteries on the nerves of the brachial plexus was a more plausible explanation   This, however, seems doubtful, for when seen again in May 1938 he stated that the pain in the arm had ceased to trouble him   He eventually died of carcinoma of the stomach at the age of 52

Case 12   A man of 27 complained of attacks of præcordial pain passing through to the back, on account of which he was suspected of aneurysm

Case 13   A storekeeper, aged 24, began to complain of pain in the back at the age of 17   Nevertheless he continued to play football regularly until twelve months before I saw him   He then gave it up, not on account of the pain, but because it made him unduly tired   The pain was most severe when he first got up in the morning and passed off in about half an hour   At the age of 22 he had a course of treatment from an osteopath over a period of 18 months and was then told he had a high blood pressure   Hence he consulted me   When I last heard of him five years later he stated that he was feeling quite well   The introspective nature of this patient made me inclined to discount his symptoms to some extent

In two of the four cases reported by King (1926) pain was a prominent symptom   One of his patients, a man of 35, complained of pain on exertion in the left side of the chest, and a year later in the right chest   In King's other patient, a man of 58, the pain was in the left supra-clavicular fossa and left shoulder   One of Evans's (1933) patients complained of pain along the left border of the scapula   In both these cases the pain corresponded in position to areas of arterial pulsation

Enlarged collateral channels might produce pain in several ways   Evans (1933) suggested

that pain in the back in patients with coarctation might be due to erosion of ribs by the enlarged intercostal arteries, like the pain produced by an aneurysm of the aorta which erodes the vertebræ, but the frequency with which well-developed rib notching is present without pain makes this explanation improbable

Pain in the arm or around the costal margin is more suggestive of root or nerve pressure This might be due either to direct pressure on nerve trunks or to pressure by the enlarged anastomotic artery where it passes through the intervertebral foramen

The importance of the spinal anastomosis in coarctation of the aorta has not been generally appreciated The vertebral artery, arising from the first part of the subclavian, reinforces the spinal arteries in which the blood flows downwards to reach the spinal branches of the aortic intercostals These pass through the intervertebral foramina There are also branches from the inferior thyroid artery which pass through the intervertebral foramina in the neck to join the spinal arteries

A patient reported by Haberer (1903) is of unusual interest in this connection Three days before admission to hospital she developed transverse myelitis from which she died three months later At autopsy it was found that the anterior spinal artery had contributed to the collateral circulation and had caused compression of the spinal cord at the level of the second dorsal segment In spite of atresia of the aorta, this woman had borne seven children

The association of the pain with exertion can be explained by the increased blood flow through the tortuous and pulsating collateral channels, and the differing sites of pain may be related to differences in the anastomotic pattern

In view of the low blood pressure in the lower limbs, one would have expected intermittent claudication to be common in patients with coarctation of the aorta, but only two of my patients complained of pain or paræsthesia in the legs—an army recruit who had played games at school, and had complained of pain in the calves on exertion since the age of 17 (Case 16) and a young woman with coarctation and a patent ductus who suffered from peculiar attacks of paræsthesia, associated with a sensation of heaviness but not actual pain in the lower limbs (Case 24)

In both cases reported by Blumgart, Lawrence, and Ernstene (1931) occasional cramp in the legs was complained of King (1926), Parsons-Smith (1921), and Woltman and Sheldon (1927) each reported a case with intermittent claudication and in Gossage's case (1913) the patient suffered all his life from weakness in the legs

CASES IN WHICH THERE WERE NO SYMPTOMS

It is surprising how many patients with coarctation of the aorta are not only free from symptoms, but reach a high standard of physical and mental development Maude Abbott refers to the case of a university professor " who presented no signs of failing circulation unless his remarkable mental development and an unusually lively and restless nature were signs of an arterial hyperæmia of the brain "

Nine of my patients were free from symptoms in May 1945 and of these 5 were over 30 years of age In addition there were 3 (Cases 6, 3, and 5) who reached the ages of 57, 50, and 45 respectively before symptoms developed Three young recruits (Cases 20 (see p 125), 22, and 25) and the following 6 older patients are known to have been symptom-free up to May 1945

Case 4 A man, now 39 years of age, who has had no symptoms directly attributable to his coarctation, was referred to me in 1937 by my colleague, Professor E D Telford, whom he had consulted on account of incipient gangrene of the terminal phalanx of the middle finger of the left hand This he attributed to an accident two years before in which the nail had been torn off examination, however, revealed a predisposing local lesion in the left arm, namely congenital phlebarteriectasis In 1938 he was admitted to the Middlesex Hospital where the affected finger was amputated When I last saw him in May 1945 he stated that since 1941 he had held a clerical job and had been off work

only one day   The left arm still ached at times and this occasionally kept him awake at night   The aching was relieved by elevating the limb   The symptoms in this case may have been entirely attributable to his phlebarteriectasis

Case 7   A business man, who is now 45, never had any symptoms apart from occasional extrasystoles   He first consulted me in 1931 as high blood pressure had been discovered in the course of a routine examination   There was nothing of significance in his medical history and he was able to play a hard game of tennis   When I last heard of him, in 1945, he stated that he had not felt better for years   He worked hard during the war, his hours were long, and he could dig for long periods in his garden—a large one which he kept entirely unaided

Case 10   This woman is living and well at the age of 39 (1945)   She was referred to me on account of thyrotoxicosis in 1938   Before this she had been very fit and during the summer of 1937 had played tournament tennis   The thyrotoxicosis was cured by a course of X-ray treatment   Since then she has been free from symptoms and during the war has engaged in Red Cross work in addition to her housework and has undertaken the active charge of a large garden which has entailed a lot of heavy digging (see p 112)

Case 17   An assistant works manager in a big industrial firm, now aged 38, consulted me in 1937 having been refused a pilot's licence on account of high blood pressure, though he had previously served in the Oxford University air squadron   He was able to play tennis and squash without the least discomfort, and during the war he became a platoon sergeant in the Home Guard, but retired after three years' service on account of insomnia, which he wisely regarded as a warning to avoid violent exertion   Since then he has had no further trouble and has been able to deal with the strenuous conditions of war-time factory management

Case 19   A dyer, aged 32, who was employed during the war as a foundry labourer, was referred to me by a medical board in 1942   All his life he had done laborious work and had never been conscious of any disability   He wrote me in 1945 saying that he still kept perfectly fit   He was working seven days a week and would have liked to get into the army

Case 23   A man, aged 27, consulted me on account of a murmur, due to a patent ductus   He also had coarctation of the aorta, but neither lesion had ever caused any disability   (See p 115)

To sum up, 9 of the 23 cases which it has been possible to follow up were free from symptoms in May 1945 and 5 of these were then over 35 years of age   In addition 3 other patients in my series did not develop symptoms till after the age of 45

To look at the problem from another angle, if one excludes the 3 who have been lost sight of, the remaining 23 in my series may be divided into three groups in accordance with their age at the present time   Three lived to over 50 years of age   All three are now dead, but two died of conditions unconnected with their coarctation, namely carcinoma of the stomach and lobar pneumonia   None of them had any symptoms before the age of 45 and one lived to 62   Between 30 and 50 there are 7 cases   Of these one died at 36, after her second confinement, the other 6 are alive and 5 have been free from symptoms up to the present time   Of the 13 cases under 30 years of age, 6 have died and 7 are living, 4 of the latter being free from symptoms

TABLE VI
PROGNOSIS OF AGE GROUPS (BRAMWELL)

	Dead	Symptoms	No symptoms	Total
Over 50	3	—	—	3
30–50	1	1	5	7
10–30	6	3	4	13
Totals	10	4	9	23

The third decade appears to be the dangerous period, and this is not surprising for it is then that the men are exposed to the greatest physical strain and the women are likely to have their first pregnancy, while subacute infective endocarditis is common at this age

The number of patients over 30 years of age who are not merely free from symptoms but able to undertake considerable physical activity suggests that when the coarctation is sufficiently well compensated to surmount the hazards of the third decade it may cause little trouble until the degenerative period of life

<div align="center">DIAGNOSIS</div>

The classical signs of coarctation are (1) high arterial pressure in the upper limbs associated with lower pressure in the lower limbs, (2) pulsating arteries on the back or front of the chest, and (3) rib notching as shown by radiography   One or more of these signs may be absent in some cases there is no clinical evidence of a collateral circulation and the ribs are not notched, and occasionally the blood pressure is not above normal

To these signs I would add two others that are unlikely to escape detection in the course of an ordinary routine examination—excessive arterial pulsation at the root of the neck and a systolic murmur, the distribution of which does not conform to that of the common valvular or congenital lesions, this murmur may be very clearly heard, in fact it is sometimes loudest, in the interscapular region   There is also a radiographic abnormality that may be of diagnostic importance when rib notching is absent—a double aortic knuckle

The Arterial Pressure   As Lewis (1934) pointed out, unless the possibility of coarctation be kept in mind in all cases of unexplained hypertension, the condition is apt to escape recognition, and palpation of the femoral pulse should be included in the routine examination of all such cases   I would add that in order to avoid missing coarctation the blood pressure in the lower limbs should be taken in all cases of patent ductus and in those cases of aortic incompetence in which the aetiology is obscure

Occasionally the blood pressure in the upper limbs is not raised   In Case 10 in my series it was 140/90 and in Case 2 it fell from 165/90 to 130/60 when subacute infective endocarditis supervened   In one of the children in my series (Case 1) in whom the coarctation was associated with subaortic stenosis the pressure was only 95/75   Hallock and Hebbel (1939) reported a case without hypertension   in one of King's (1937) cases the blood pressure was only 123/87 and in Case 12 of Blackford's (1928) series, a man of 24 who had served in the American Navy, the pressure was 128/88

The Collateral Circulation   The collateral circulation in coarctation of the aorta was first described by Paris in 1791   Unless the back and front of the chest be inspected carefully in a good light, pulsating arteries can easily be overlooked   In one of my patients (Case 9) in whom the collateral circulation had been quite obvious when the heart rhythm was normal, pulsation could only be detected by very careful palpation when auricular fibrillation supervened

A late systolic murmur is generally audible over the dilated arteries that form the collateral circulation and may be heard on the back of the chest even when no pulsation is palpable   When the internal mammary and deep epigastric anastomosis is well developed, the peculiar distribution of the murmur, which is equally well heard on both sides of the chest in an area parallel to the border of the sternum, can hardly fail to attract attention

The superficial anastomosis is no sure indication of the extent of the anastomosis as a whole In Case 8 in our series, which came to autopsy, one of the most important anastomoses proved to be between the superior intercostal, arising proximal to, and the aortic intercostals, arising distal to the coarctation   This anastomosis is deeply situated and is inaccessible to palpation It is not surprising that these vessels should be greatly dilated since they provide the shortest route to circumvent the coarctation, and when this route is freely patent the femoral pulse may be of good volume even though there be complete atresia of the aorta   When on the other hand the blood has to follow a more circuitous route to reach the descending aorta, the volume of the femoral pulse is correspondingly reduced, for, as Bonnet pointed out, the

sensation conveyed to the finger by palpation of the pulse depends, not on the blood flow, but on the steepness of the pressure gradient along the front of the pulse wave the volume of the femoral pulse bears no relation to the degree of stenosis of the aorta

In normal subjects the femoral and radial pulses are synchronous on palpation, but in many cases of coarctation the femoral pulse appears to be delayed This is due to the fact that it is not the arrival of the pulse wave in the artery, but the crest of the wave that is appreciated on palpation and, in coarctation, the pulse in the lower limb is of the slowly rising type

Other problems relating to the collateral circulation are more fully discussed in our previous paper (Bramwell and Jones, 1941)

Radiological Diagnosis

The discovery that rib notching could be demonstrated radiographically was a great stimulus to the diagnosis of coarctation of the aorta Prior to the publication of Roesler's paper very few cases had been recognized during life Rib notching does not occur in every case, and is absent when the coarctation is associated with a freely patent ductus arteriosus Well-developed rib notching was present in 17 of the cases in my series in 5 (Cases 11, 17, 20, 21, 22) it was not sufficiently definite to be of diagnostic value and in 4 it was absent, two of these (Cases 1 and 18) were children and in 3 of the 4 (Cases 18, 23, and 24) the ductus was patent

Laubry's (1937) suggestion that rib notching is not pathognomonic of coarctation led us to make further observations on the point These have convinced us that the trivial degree of notching occasionally met with in other conditions is easily distinguished from the notching of coarctation

The absence of the aortic knuckle has been stressed by most writers as an important radiological sign the vascular pedicle being funnel shaped, but, although this is a striking feature in some cases, in others, prominences that may easily be mistaken for the aortic knuckle are produced by other structures

Direct demonstration of discontinuity of the aorta with the patient in the left oblique position is theoretically the most convincing proof of coarctation, but in our experience this is rarely possible even by the use of tomography Fray (1930) states that a defect in the aorta can be demonstrated in all cases in which it is possible to obtain a satisfactory left oblique film, but his statement appears to be based on only two cases Taylor (1934), on the other hand, was unable to demonstrate discontinuity in any of her five cases, Roesler (1943) agrees that it is sometimes impossible, especially in young subjects, and Brown (1939) states that even in the adult it can rarely be demonstrated

When rib notching is absent, the most important radiological sign of coarctation is the presence of a double prominence in the region of the aortic knuckle (Fig 4 and 7), the upper component being formed by the dilated left subclavian artery where it arises from the blind end of the aorta proximal to the coarctation, and the lower component by the blind end of the descending aorta This and other aspects of the radiological diagnosis will be more fully discussed in a subsequent paper

In five of the cases in the present series the diagnosis was made by the radiologist (Table VII) In one (Case 6) the clinical signs were attributed to associated aortic regurgitation, in another (Case 10) in which the blood pressure was only 140/90 to Graves's disease, while in a third (Case 1) they were overshadowed by those of subaortic stenosis It is in cases such as these, in which some additional lesion is present, that coarctation is especially liable to be overlooked The other two cases were referred to me by my colleagues after the condition has been diagnosed radiologically —Case 5, with pain in the arm which it was thought might

TABLE VII

Cases Diagnosed by Radiology

Case	Sex	Age	Clinical diagnosis	Radiology
6	M	58	Aortic incomp	Rib notching
10	F	31	Thyrotoxicosis	Rib notching
1	M	9	Subaortic stenosis	Double knuckle
5	M	46	? Cervical rib	Rib notching
12	M	27	? Aneurysm	Rib notching

be due to a cervical rib, and Case 12, where the physical signs suggested the possibility of aneurysm of the aorta

In Case 6, aged 58, the heart was greatly enlarged, he had an aortic diastolic murmur, and the blood pressure was 200/80   No subcutaneous arterial anastomosis was detected, but X-ray examination showed notching of the ribs and absence of any aortic knuckle or aortic impression on the œsophagus   Clinically this appeared to be a straightforward case of aortic incompetence with auricular fibrillation, but there was one feature that should have led us to suspect coarctation—the high systolic pressure   In aortic incompetence due to rheumatic infection, syphilis, or arteriosclerosis, the systolic pressure rarely exceeds 170

In Case 10, referred on account of thyrotoxicosis, arterial pulsation in the neck was excessive but this did not arouse my suspicion, as I attributed it to the overacting heart, and the blood pressure was only 140/90   I referred her to Dr E W Twining for X-ray treatment and it was he who made the diagnosis   Thinking that the carotid pulsation was more than could be accounted for by the thyrotoxicosis, he took a film of the chest which showed typical rib notching   This was the only adult patient in my series in whom the blood pressure was not at any time found to be above normal

The association of thyrotoxicosis with coarctation is interesting   Cookson (1936) who reported a case of coarctation of the aorta with toxic goitre, treated by complete thyroidectomy, suggested that the association is too frequent to be fortuitous   In support of this hypothesis, he refers to papers by Loriga (1887), Blackford (1928), Ulrich (1931), Amberg (1932), Eppinger and Midelfart (1933) and Brown (1934)   Of the 9 cases reported by these authors, 7 were females   Cookson suggests that the mechanism by which thyroid disturbance arises in association with coarctation is the increased blood supply to the gland, as a result of the collateral circulation through the superior and inferior thyroid arteries which arise from the external carotid and subclavian respectively, above the coarctation

In the fifth case, diagnosed by radiology (Case 1), the apical cardiac impulse was in the anterior axillary line and a second impulse and systolic thrill were palpable to the right of the manubrium   A to-and-fro murmur was audible over the manubrium and a systolic murmur on the back of the chest   The blood pressure was 95/75 and the femoral pulse was of good volume   Dr Evan Bedford kindly gave me his opinion on the interpretation of the unusual X-ray appearances in this case (Fig 4)   He considered that the double aortic knuckle signified coarctation of the aorta, the upper knob corresponding to the blind end of the aortic arch and the lower one to the blind end of the descending aorta   My colleague, the late Dr E W Twining made an exhaustive tomographic investigation of this case and satisfied himself that this explanation was correct   I have since been struck by the extraordinary similarity of this radiogram to that in Hamilton and Abbott's (1928) case

COARCTATION ASSOCIATED WITH PATENT DUCTUS

The diagnosis of coarctation when associated with a patent ductus may be very difficult

FIG 4 —Radiogram Case 1, showing double aortic knuckle (see text)

The first case was diagnosed post-mortem, the second clinically, and in the third, a child, the diagnosis was suspected

Case 24   An unmarried woman, aged 23, was admitted to hospital from my outpatient clinic on November 26, 1941, complaining of dyspnœa and œdema of the feet   She had been short of breath as long as she could remember and cyanosed in cold weather since birth   These symptoms had been worse during the past year   In July 1941 she had been admitted to Withington Hospital with retention of urine and acute respiratory distress and I am indebted to the Medical Superintendent, Dr Greenwood, for information regarding her condition at that time   She then had œdema of the feet and complained that she had " no use in her legs "   Her symptoms were relieved by catheterization

The heart shadow (Fig 5) was globular with generalized cardiac enlargement, but no rib notching   Auscultation revealed triple rhythm at the apex and a harsh murmur extending from systole into diastole, but chiefly diastolic, maximal in the third left intercostal space close to the sternum.   Moist sounds were present at the bases of the lungs, and the liver was slightly enlarged   Her systolic pressure was 170, but the diastolic end-point was indefinite

On November 28 she complained of tingling starting in the left foot, then affecting the right foot, spreading up to the thighs, and also involving the left arm   This symptom had occurred on previous occasions   It was associated with a feeling of constriction in the lower sternal region   The legs felt heavy, but were not actually painful, and during the attack the dyspnœa and cyanosis were accentuated   All pulses were palpable in the arms and legs, but that in the dorsalis pedis was very feeble   Catheterization again relieved her symptoms and on the following day her condition had returned to normal   On December 1, she had another similar attack with paræsthesia in the lower part of the body   This time catheterization and morphia gave only incomplete relief   Her condition progressively deteriorated and she died three days later

The weight of the heart post-mortem was 600 g   Both right and left ventricles were greatly

ʜ

Fig 5 —Radiogram Case 24 showing a globular heart with general enlargement, but no rib notching

Fig 6 —Autopsy specimen Case 24   Aorta, pulmonary artery, and patent ductus arteriosus

hypertrophied but their cavities were not dilated   The right auricle was hypertrophied but the left auricle appeared normal   The ductus arteriosus was widely patent (Fig 6)   The diameter of the aorta at its origin was normal, but at the point of coarctation between the left subclavian and the ductus it would barely admit a pencil

Coarctation had not been suspected in this case, though the peculiar paræsthesia in the legs should have aroused our suspicion   Since then in every case of patent ductus I have looked for evidence of coarctation, but hitherto I have found it only once

FIG 7 —Radiogram Case 23 with coarctation and patent ductus arteriosus

Case 23   A municipal civil servant, aged 27, consulted me because he had been rejected for another post on account of a cardiac murmur   It was the typical machinery murmur of patent ductus The blood pressure in the arm was 165/80, but the systolic pressure in the dorsalis pedis was only 115 I, therefore, suspected the possibility of coarctation   There were no pulsating arteries on the back or front of the chest and radiography showed no rib notching, but it did show a double prominence in the region of the aortic knuckle (Fig 7) and on screening it was obvious that the upper knob pulsated violently whereas the pulsation in the lower knob was feeble, the former being proximal and the latter distal to the coarctation

Case 18   A boy, aged 11, was seen in consultation in September 1936   He had been a promising

athlete for his age and very fit until taken ill at school in July with a pain in the left thigh   Three weeks later he was admitted to a nursing home with a swinging temperature and an enlarged spleen From August 10 until I saw him the temperature had been normal, but on September 8 he complained of a pain in the left chest and his pulse rate increased from 80 to 116 and subsequently remained rapid

He had a systolic murmur both at the apex and at the base of the heart   The murmur was also clearly audible on the back of the chest   The blood pressure was 140/90   The spleen was easily palpable and he was considered to be suffering from subacute infective endocarditis   Progress was satisfactory till May 1937 when again after a motor ride, his temperature rose to 99 4° F and for a few days he had epistaxis   Subsequently, from time to time, he had pains in the chest, foot, shoulder, and other places, each associated with a rise of temperature

FIG 8 —Radiogram Case 18, with coarctation and patent ductus arteriosus (August 20, 1937)

He was admitted to my ward on August 11, 1937, and it was then found that no pulsation could be felt in the femoral arteries   X-ray examination of the chest (Fig 8) by Dr Twining showed enlargement of the blind end of the descending aorta and enlargement of the pulmonary conus, but no rib notching   Dr Twining suggested that the radiograms probably indicated coarctation of the aorta associated with patent ductus   Blood culture yielded a profuse growth of *Streptococcus viridans* This was repeated and confirmed   He was treated with prontosil, but without benefit   On September 18 he developed a dry cough and the air entry in the left lung was found to be diminished   X-ray examination on September 25 showed partial collapse of the left lower lobe and on October 13 complete collapse of the left lung (Fig 9)   The pulmonary complications in this case suggested that the infection involved the ductus as well as the aortic valve

FIG 9 —Radiogram Case 18, showing collapse of left lung (October 13, 1937)

PROGNOSIS

The number of cases in my series is too small to enable me to draw any firm conclusions regarding prognosis, but certain general deductions appear to be justified   In May, 1945, 10 of my patients were over 30, while 16 were under 30 years of age   Of the latter 3 have been lost sight of   In the older group 4 are dead, in the younger group 6   Of the 4 fatal cases in the older group 3 lived to over 50 years of age and in 2 of these death was not attributable to the coarctation, 1 died of carcinoma of the stomach and the other of lobar pneumonia   Of the remaining 6 patients in this group 5 are not merely alive but free from symptoms   One woman (Case 26) has passed safely through two pregnancies, one man (Case 4) is in a clerical post, and the other 4 all indulge in strenuous physical work   Symptoms dated from childhood in 4 of the 6 fatal cases in the younger group

It would appear, therefore, that patients whose symptoms date from childhood are unlikely to reach the age of 30, whereas in those who are free from symptoms until the age of 30 the further expectation of life is much more favourable they have passed safely through the hazards of the third decade

To the two groups considered above there must be added a third with which I am not concerned in this paper, since young children do not figure in my series   Sixteen of the 28 patients in Evans's (1933) series died in infancy and in 15 of these the coarctation was associated with a patent ductus (see Table I)

Of 82 cases of coarctation collected by Abbott, in which death occurred within the first year, 50 exhibited some major congenital anomaly such as bilocular or trilocular heart, transposition of the arterial trunks, or pulmonary atresia   In the great majority of cases in which death occurs in infancy the coarctation is of the " infantile " type   These cases are of more interest to the embryologist than to the clinician

It is interesting to compare the expectation of life in my series with that in the series of cases collected by Maude Abbott Of her 200 cases, 103 (51 per cent) died before the age of 30 and a further 45 making a total of 148 (74 per cent) before the age of 40 In round figures, therefore, half her cases died before 30 and another quarter before 40 Thus between the
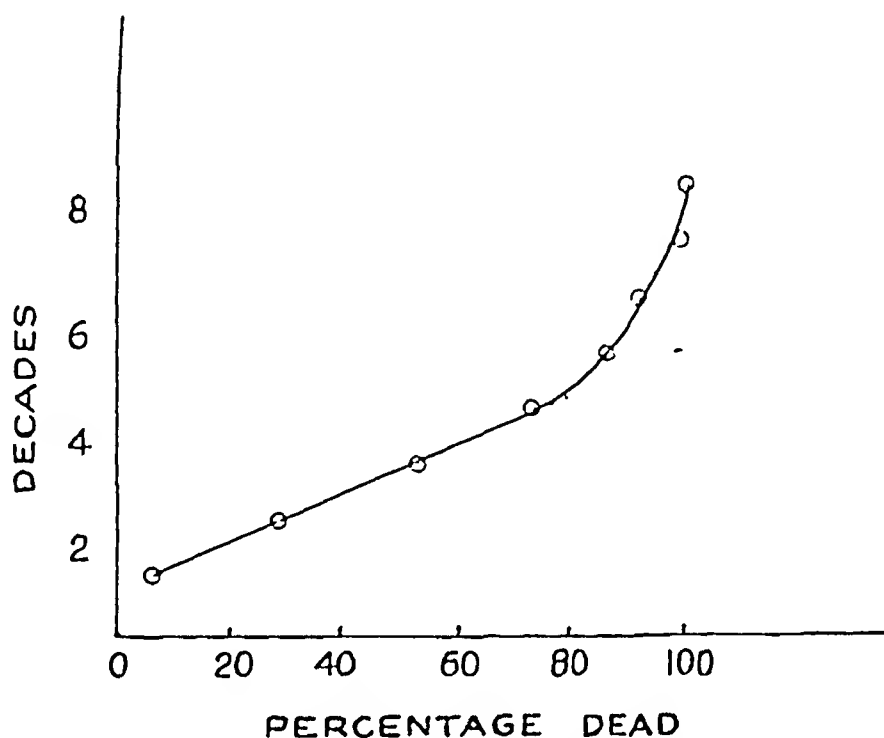

Fig 10 —Graph showing age and mortality of coarctation of the aorta from Maude Abbott s series

ages of 10 and 40 there is practically a linear relation between age and death-rate (Fig 10) Had this been continued after 40, as shown by the interrupted line, all Abbott's cases would have been dead by the age of 50, but after 40, the death-rate tends to fall off, for in patients who reach 40 the coarctation often causes little serious disability, survival for a considerable period of years is not unlikely, and death not infrequently is due to some cause unconnected with the coarctation

Blackford's figures are very similar to Abbott's Of 180 cases over 5 years of age, 76 (42 per cent) died between the ages of 16 and 30 and 36 (20 per cent) between 30 and 40 Blackford states that many of these were young athletes who died during or shortly after exercise

Cause of Death

The cause of death in the 10 fatal cases in my series is shown in Table VIII Four died of congestive heart failure, 2 of subacute infective endocarditis, and 1 of each of the following conditions, septicæmia, subarachnoid hæmorrhage, carcinoma of the stomach, and lobar pneumonia

Deaths from congestive heart failure occurred at the ages of 11, 23, 36, and 52 The other fatal cases fall in two well-defined age groups The three patients who died of cardiovascular causes and the one who died of septicæmia were all under 30, whereas the two who died of

TABLE VIII

CAUSE OF DEATH (BRAMWELL'S SERIES)

Case No	Age at death	Cause of death	Remarks
1	11	Congestive heart failure	Subaortic stenosis
18	12	Infective endocarditis	Patent ductus
2	23	Infective endocarditis	
15	23	Septicæmia	
24	23	Congestive heart failure	Patent ductus
8	27	Subarachnoid hæmorrhage	
9	36	Congestive heart failure	Two pregnancies Auricular fibrillation
3	52	Congestive heart failure	
5	52	Carcinoma stomach	
6	62	Lobar pneumonia	Auricular fibrillation

causes unconnected with their coarctation were both over 50   This suggests that in patients who survive the hazards of the first three decades the chief danger of coarctation is congestive heart failure

Subacute infective endocarditis is a well-known complication of congenital heart disease, but the risk of subarachnoid hæmorrhage from rupture of a cerebral aneurysm has not received adequate recognition   Abbott believed that, in young subjects without history of trauma or infection, spontaneous subarachnoid cerebral hæmorrhage was usually due to a ruptured cerebral aneurysm of congenital origin   This was shown at autopsy to be the cause of death in 5 of her cases and she pointed out that the early age of the patients, the large collateral circulation, and the history of repeated small cerebral hæmorrhages suggested that the same was probably true of the other 13 cases of spontaneous cerebral hæmorrhage in which no aneurysm was actually demonstrated

TABLE IX

CAUSE OF DEATH (ABBOTT AND BLACKFORD)

	Abbott	Blackford
Rupture of heart or aorta	44	38
Myocytic endarteritis of aorta	10	—
Cerebral lesion	24	25
Gradual heart failure	60	68
Sudden heart failure	17	16
Total deaths from cardiovascular causes	155	147
Total number of cases in series	200	196

Maude Abbott and Blackford both found that death was due to cardiovascular causes in over 70 per cent of the cases which they analysed (Table IX)   My small series differs from those of Abbott and Blackford in that in no case was death due to rupture of the aorta, a complication that proved fatal in about 20 per cent of their cases   Three of Lewis's cases (Table X) died suddenly at the age of 31, 42, and 49, respectively, but in none of these was the cause of death determined, although in one a post-mortem examination was performed.

An associated congenital abnormality that appears important as a predisposing cause of death is a bicuspid aortic valve   This abnormality not only renders the patient more liable to subacute infective endocarditis but is frequently associated with a congenital weakness of

the aortic wall   A bicuspid aortic valve was present in 22 per cent of the cases in Abbott's series and in over 50 per cent of those in which death was due to spontaneous rupture of the aorta

An aortic diastolic murmur was detected in only 4 of my patients (Cases 1, 3, 6, and 15) Perlman, on the other hand, reported a diastolic murmur in 10 of his 13 cases   This very high incidence is difficult to explain unless he applied the term " diastolic " to what other workers call a " late systolic " murmur.

Hazards of Coarctation

Bonnet (1903) maintained that fully compensated obstruction of the thoracic aorta made no extra demand on the cardiac reserve, and that hypertrophy of the heart was never present in uncomplicated cases   Lewis (1933) held the view that prolonged overwork in itself never led to heart failure   Abbott (1928) on the other hand believed that uncomplicated coarctation did entail cardiac strain which might by itself lead to death from failing compensation   She quotes a large number of observations in support of this hypothesis, and she found that cardiac hypertrophy was present in 75 per cent of the 200 cases she reviewed

A detailed statement concerning cardiac enlargement in my own cases will be given in a later paper dealing with the radiology of coarctation   Here let it suffice to say that gross cardiac enlargement was present in only 4 of my 26 cases   in 3 of these (Cases 1, 3, and 6) it was associated with aortic incompetence and in the fourth (Case 24) with a freely patent ductus

Case 2 is of particular interest in that we were able to compare the cardio-thoracic ratio at the age of 11 and 21   No alteration had occurred   Lewis (1933) reported little if any increase in heart size in those of his cases that were under observation for several years These were older men   in my case there was no relative increase in heart size over the period of active growth

My own observations lead me to believe that coarctation of the aorta does impose an additional load on the heart which entails a corresponding reduction in the cardiac reserve, but that, in the adult type of coarctation, this alone is not sufficient seriously to embarrass the heart during the first half of life, nor to render it incapable of meeting its everyday commitments   When coarctation is not complicated by the presence of some other heart lesion, symptoms of circulatory insufficiency are not likely to supervene unless the heart muscle be weakened by intercurrent infection, or an additional burden be imposed upon the heart by severe physical strain, in which case a progressive deterioration in health may ensue

Not infrequently patients date their symptoms from some intercurrent infection which appears permanently to have upset the equilibrium   This is clearly illustrated by Lewis's series of cases of coarctation amongst pensioners from the First World War   These men had been invalided out of the army on account of cardiovascular symptoms and it is interesting to note the various conditions that were responsible for their breakdown   In three (Table X) symptoms of circulatory insufficiency developed following an attack of malaria   One (Case 3) developed symptoms at the age of 19 following an attack of P U O which from Lewis's description sounds like trench fever   In a fifth (Case 6) a man of 27, who had served three years in the army, symptoms followed a foot infection   Thus in 5 of Lewis's 8 cases the onset of symptoms was attributable to intercurrent infection   There is, however, little evidence that a progressive cardiovascular deterioration occurred as the result of such infection since all five men survived for more than 10 and one for 24 years   This patient was 63 at the time Lewis's paper was published and subsequently attained the age of 73

I am indebted to Dr E E Pochin for the further history of this remarkable case, who was under treatment by Sir Thomas Lewis in October 1942 with increasing breathlessness over the

TABLE X

LEWIS'S CASES FROM THE 1914–18 WAR

Case	Predisposing cause	Age first symptom	Remarks	Dura-tion	Age at death	Cause of death
				(years)		
1	3 months' training	19	Previously active	12	31	" Sudden "
6	Foot infection	27	3 years' service	15	42	" Sudden "
7	Malaria	33		10	43	Infective endocarditis C H F (P M)
8	After 4 months' France	41	Previously reserve	8	49	" Sudden " (P M)
4	Cycle accident	40	Detached retina	12	52	C H F auricular fibrillation
5	Malaria	49	Rejoined 1914 aged 47	12	61	Acute pneumonia
2	Malaria	49	Enlisted 46 R F A 3 yrs foreign service	14+	—	Living 63*
3	P U O	19	14 months front line, football	17+	—	Living 36

* Died 1944, aged 73

previous twelve months and with several attacks of loss of consciousness during the preceding few weeks   He then could not walk more than 200 yards without having to stop owing to breathlessness and was made breathless by one flight of stairs   The attacks of unconsciousness occurred shortly after waking and were continued in hospital where he was found to have heart block   The degree of block was variable, some records showing a long P–R interval with a 1 1 ventricular response, most showing 2 1 block with a ventricular rate of about 44 with some failures of ventricular response and some extrasystoles, while some records showed complete heart block

He had at this time 4 cm of venous congestion, the cardiac apex beat was 15 cm to the left in the fifth space, the right border of dullness being 4 cm to the right of the mid-line   The blood pressure was 200/120 in the arms and 80/60 in the legs   On treatment with ephedrine his Stokes-Adams attacks ceased and his heart rhythm became regular at a rate of about 80, but he still showed alternation of the pulse and gallop rhythm   He was seen at intervals until October 1944 when he died, out of hospital   No details of his form of death are available, but a post-mortem was obtained and the specimen is now in the Pathological Department of University College Hospital

Severe physical strain is another hazard to which these patients are liable to be exposed, for as Abbott points out the majority are males and many are of an athletic, muscular build Blackford (1928) states that in many cases sudden death from rupture of the aorta has occurred during or immediately after athletic exertion

Pregnancy and Coarctation

A correct appreciation of the dangers of childbirth in women with coarctation is important, since grave complications are liable to develop unexpectedly during the second stage of labour Two* of the patients in my series have been under observation during pregnancy

Case 26   A woman aged 37 was referred to my clinic in the fourth month of her second pregnancy on account of a history of mitral stenosis   She was delivered by Cæsarean section in August 1945 and when last seen in August 1946 was well except for slight breathlessness on exertion   Up to the age of 20, when she first consulted a doctor on account of breathlessness when cycling and œdema of

* Two other cases seen since May 1945 have been successfully delivered by Cæsarean section

the ankles, she had been perfectly fit A heart murmur was discovered at that time This was wrongly attributed to mitral stenosis and she was accordingly kept in bed for six weeks Subsequently, until her marriage at the age of 24, she worked as a machinist and lost little time off work through ill health, but strenuous exertion made her breathless Convalescence following her first confinement—a forceps delivery at the age of 29—was prolonged and she was in bed for six weeks, but from then onwards she enjoyed good health until she again became pregnant Apart from her illness at the age of 20, which appeared to be attributable to over-exertion, this woman had little in the way of symptoms except during her two pregnancies

Case 9 —A primigravida, aged 31, was admitted to St Mary's Hospital, Manchester, with a view of Cæsarean section for contracted pelvis, and was referred to my clinic in March 1933 on account of high blood pressure She had been unaware of any heart trouble up to the fourth month of pregnancy when she had noticed some shortness of breath and palpitation For sixteen years before her marriage at the age of 29, she had worked hard on a farm where her daily routine included heavy lifting and scrubbing

She was successfully delivered by Cæsarean section in April 1933 Six weeks later she developed a severe hypochromic anæmia which responded well to treatment and she then remained free from symptoms until November 1935 when she began to complain of lassitude, palpitation, and præcordial pain on exertion On examination it was found that she was again pregnant and had developed auricular fibrillation In May 1936 she had a complete abortion from which she made a good recovery, but subsequently she developed congestive heart failure from which she died in May 1938 This case has already been fully reported (Bramwell and Longson, 1938)

A case reported by Walker (1943) presented some similarity to the one described above She also was a farmer's wife, 31 years of age, but before marriage her activities had been considerably restricted She remained fit throughout pregnancy and tolerated the first stage of labour well, but became acutely distressed and breathless following rupture of the membranes She was delivered by forceps and convalescence was uneventful

The alarming complications that may develop unexpectedly during labour are illustrated by a case reported by Billinghurst (1943) His patient, a healthy and athletic primipara of 23, who had no symptoms during pregnancy, fainted at the onset of the second stage of labour and died suddenly the day after delivery from rupture of the aorta

TABLE XI

JENSEN'S CASES OF COARCTATION ASSOCIATED WITH PREGNANCY

Author	Date	Age	No of children	Remarks
Leudet	1858	37	4	Died from rupture of aneurysm just beyond coarctation
Kreigh	1878	28	2	Died following stroke in 9th month of her 3rd pregnancy
Fawcett	1905	45	9	Died of congestive heart failure 14 days after induction of premature labour
Abbott	1915	38	1	Died of congestive heart failure some years after confinement
Katz	1921	25	1	Died on rupture of the aorta near the end of 2nd pregnancy
Strassmann	1922	56	7	Found dead in bed
Strayhorn	1937	26	0	Successfully delivered by Cæsarean section

In 4 of the 7 cases collected by Jensen (1938) (Table XI) death occurred either during pregnancy or shortly after delivery from causes directly related to the coarctation but one of these women had survived eight previous pregnancies and another lived to the age of 56 after having had seven children

SUMMARY AND CONCLUSIONS

Twenty-six cases of coarctation of the aorta are reported   In 20 the diagnosis was based on clinical evidence, in 5 it was made by the radiologist, and in 1 the lesion was discovered post-mortem

The classification, clinical manifestations, and prognosis of the condition are discussed and the following conclusions are reached

Coarctation of the aorta is apt to escape recognition, unless the possibility of the condition be continually kept in mind   Many of Lewis's cases were under observation for years before they were correctly diagnosed   When associated with a patent ductus or with aortic incompetence, coarctation is especially liable to be overlooked

Clinically the diagnosis is based on the finding of high systolic blood pressure in the upper limbs associated with low pressure in the lower limbs, pulsating arteries on the back or front of the chest, excessive arterial pulsation at the root of the neck, and a late systolic murmur of abnormal distribution   The most important radiological manifestations are rib notching and occasionally a double aortic knuckle   Direct demonstration of the coarctation is rarely possible   Diagnosis is most difficult when the ductus is patent, for then there may be no collateral circulation and no notching of the ribs

In many cases, symptoms first appear following some intercurrent infection or physical strain   Dyspnœa, palpitation, and fatigue are the most common complaints   Pain in the trunk and arms may be due to pressure on nerves by the dilated arteries participating in the collateral circulation   The spinal anastomosis is of importance in this connection

Despite a deceptively good exercise tolerance, a sudden strain may prove fatal even in the prime of life   these patients are living dangerously   It is accordingly wise to limit their activity   Women with coarctation should be delivered by Cæsarean section

In coarctation of the aorta fatal complications are so liable to develop unexpectedly that prognosis is extremely uncertain   a patient who appears to be in robust health one day may be dead the next

Patients in whom symptoms date from childhood rarely live to 30, whereas those who surmount the hazards of the first three decades may suffer little disability from their coarctation The efficiency with which the circulation may be maintained year after year, in spite of the increased load due to high blood pressure, is remarkable

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APPENDIX

Two patients in this series who were alive in May 1945 have since died   Their subsequent history and the post-mortem findings were as follows

Case 13   This man was admitted to the Bolton Royal Infirmary on 15/10/45 suffering from subarachnoid hæmorrhage from which he made an uneventful recovery   He was readmitted on 9/12/46 following a severe hæmoptysis   His blood pressure then was 130/70   During the ensuing week three further hæmoptyses occurred, and he died on 16/12/46

I am indebted to Dr Horace Jackson for the further clinical history in this case and for the following report on the post-mortem examination   There was a cavity filled with fresh blood clot in the lower lobe of the right lung and the surrounding tissue was saturated with blood   The hæmorrhage appeared to have resulted from rupture of a fairly large vessel, but there was no clear evidence of an aneurysm   There was no tuberculosis   Just distal to the origin of the left subclavian artery, at the point of insertion of the ductus, which was closed, the aorta was narrowed, but not completely occluded (Fig 11 on p 126)   It admitted a probe 0 2 cm in diameter   The internal mammary vessels were very large   Examination of the brain revealed an aneurysm about 1 cm in diameter on the circle of Willis   The surrounding brain showed staining from an old hæmorrhage—probably that from which the patient suffered in 1945

Case 20   This young man kept well until April 1946 when, after rowing, he had an attack of sweating, and for three days was febrile, complaining of pain in the right thigh and right foot   Four weeks later he had another febrile attack, again after rowing   He was then seen by Dr D Rhodes Allison who diagnosed subacute bacterial endocarditis and admitted him to a private ward at the Manchester Royal Infirmary on 7/6/46   I am indebted to Dr Allison for the opportunity of seeing this patient at that time and for the further particulars of his illness   He was treated with penicillin and progress was satisfactory until 27/6/46 when he complained of pain in the chest   Two days later he vomited copiously and from that time his condition steadily deteriorated   On 2/7/46 he collapsed suddenly and died

Post-mortem examination by Dr F A Langley showed a narrowing of the aorta just proximal to the insertion of the ductus arteriosus which was closed, the lumen of the aorta at this point being less than 0 5 cm in diameter, whereas that of the descending aorta was 1 0 cm in diameter (Fig 12 on p 127) Beyond the coarctation, for a distance of 3 cm the wall of the aorta was much thickened and roughened and small vegetations were present   The internal mammary artery and its branches were very large   They did not directly anastomose with the deep epigastric artery but broke up into small muscular vessels in the rectus abdominis just above the umbilicus   The heart weighed 700 g , the left ventricle being greatly dilated   The interventricular septum was displaced to the right reducing thereby the capacity of the body of the right ventricle (Bernheim's syndrome)   The conus of the right ventricle was dilated   The right auricle was dilated and its wall somewhat thickened   The left auricle appeared normal   The aortic valve was bicuspid, both coronary arteries arising from the anterior sinus of Valsalva, the anterior cusp was thickened and on it there were a few small vegetations, the posterior cusp had a large vegetation covering its ventricular surface   The coronary arteries appeared normal

I am indebted to the Department of Pathology of the University of Manchester for the photographs of the post-mortem specimens

FIG 11 —Specimen of coarctation from Case 13

FIG 12 —Specimen of coarctation from Case 20

THE HEART IN TOXÆMIA OF PREGNANCY

BY

PAUL SZEKELY AND LINTON SNAITH

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Although acute pulmonary œdema is a recognized complication of toxæmia of pregnancy, its mechanism is incompletely understood   In some of the reported cases the clinical picture was similar to that of cardiac asthma and the cause of the pulmonary œdema was thought to be left ventricular failure   Detailed studies of the heart in toxæmia of pregnancy, however, have been few, and reports showing that toxæmia of pregnancy may be associated with myocardial damage are not many   Some of the cases of acute heart failure reported in late pregnancy and in the early puerperium in patients who had no signs of antecedent cardiovascular disease may have been instances of toxæmia with associated myocardial damage Thus, Blacker (1907) and later Campbell (1923) noticed the occurrence of heart failure during and after pregnancy, and in the absence of a valvular lesion they regarded myocardial disease as the possible cause for it   Herrmann and King (1930) called attention to " significant types of cardiac failure occurring in pregnant patients with non-valvular heart disease "   Toxæmia was apparently present in some of their patients

Eufinger and Molz (1936) undertook a cardiographic study of 23 cases of toxæmia of pregnancy, but were unable to demonstrate myocardial disease   Gouley, McMillan, and Bellett (1937) observed heart failure and T wave changes in the cardiogram shortly after delivery   Some of their patients died, and the histological examination showed focal myocardial necrosis, the coronary arteries were found to be normal   In two of the cases the blood pressure was raised, but in only one surviving case was toxæmia described by the authors Teel, Reid, and Hertig (1937) reported 6 cases of toxæmia of pregnancy complicated by cardiac asthma and pulmonary œdema, one came to autopsy, and the histological sections of the heart showed œdema of the stroma and occasional cellular infiltration, with slight subendocardial fibrosis and occasional thickening of the internal elastic membrane of the smaller coronary branches   They concluded that the œdema and the leucocytic infiltration of the myocardial tissue were consistent with an acute process that could have interfered with the cardiac function   Hull and Hidden (1938), reporting on the occurrence of post-partum heart failure, mentioned toxæmia of pregnancy and nutritional deficiency as possible ætiological factors, hypertension with a systolic pressure above 150, was present in one third of their cases   Thomson, Cohen, and Hamilton (1938) studied chest lead cardiograms in pregnancy, including normal subjects and patients with heart disease or toxæmia, and found that an upright T wave was usual in toxæmic patients (they used the old method of recording chest leads, according to which the T wave was normally inverted)   the R wave was entirely absent or less than 2 mm in some of the toxæmic and cardiac patients, but never in the normal cases   Bradford (1939) stressed the danger of cardiac decompensation in acute pre-eclampsia According to Dexter and Weiss (1941) and Dexter *et al* (1943), the heart is usually normal when toxæmia is mild, but severe toxæmia with generalized œdema is frequently associated with

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heart failure   They found changes in 2 of 12 cardiograms, and in both the changes appeared in the post-partum period, on the 6th and 9th day respectively   in the second the cardiogram was normal 7 days before term when signs of heart failure were present, and it became abnormal later when the failure had subsided   Dieckmann (1942) stated that patients with mild toxæmia rarely showed evidence of cardiac damage, but those with severe pre-eclampsia and eclampsia usually had tachycardia and occasionally developed heart failure   Recently Wallace, Katz, Langendorf, and Buxbaum (1946) studied the cardiogram in 12 cases of pregnancy toxæmia and found changes similar to those seen in anterior myocardial infarction in 2, both of which had heart failure, 4 showed alterations in the T wave and prolonged A–V conduction, but no clinical evidence of heart failure, and in the remaining 6 there was neither clinical nor cardiographic evidence of cardiac involvement

PERSONAL OBSERVATIONS

The present paper is based on the observations made in 19 unselected cases of toxæmia of pregnancy, delivered in the Department of Obstetrics of the Newcastle General Hospital   Although the difficulty of assessing the severity of the toxæmic state is fully recognized, an attempt has been made to classify the cases for the purposes of this study   The majority were classified as severe, the criteria being subjective symptoms, such as headache, vomiting, and visual disturbance, and height of blood pressure, œdema, albuminuria, and the occurrence of eclamptic fits   All the " severe " cases had a blood pressure of more than 160/100, in addition to other symptoms and signs of toxæmia, except one with a blood pressure of 130/95, classified as severe because of eclamptic convulsions

Clinical and cardiographic studies were made in all and, in addition, radioscopic examination in 9 cases   The cardiovascular findings are summarized in Table I   A total of 7 cases were thought to show significant clinical and/or cardiographic changes   Left ventricular failure was observed in 3 (Cases 1, 13, and 19), and the first of these also showed T wave changes similar to those seen in anterior myocardial infarction   Significant cardiographic changes were seen in 5 (Cases 1, 8, 11, 17, and 18), these changes consisting of transient alterations of the T waves usually in both standard and chest leads (Fig 1–5)   Cardiographic changes of doubtful significance were observed in 6 others   In the remaining 8 the cardiograms were within normal limits   Sinus tachycardia was frequent and extrasystoles were observed in 2 (Cases 17 and 19)

Case 1, para 3, aged 36   Admitted on 17/7/42 with œdema of the legs, albuminuria, and a B P of 185/120   She had a normal labour and was delivered on 24/7/42   Three days later she developed acute pulmonary œdema   There was marked tachycardia, triple rhythm, and slight papillœdema   The cardiogram (Fig 1A) showed inverted T waves in the limb leads   The clinical condition gradually improved, the triple rhythm disappeared, and on 18/8/42 she had no signs of cardiac failure, no albuminuria, and no œdema   Her B P was 145/95   However, the cardiogram (Fig 1B) was still very abnormal, showing inverted T wave in leads I, II, and IV   Radioscopic examination showed a normal-sized heart   On 4/9/42 the B P came down to 140/90   Repeated cardiograms were done, and a gradual increase in the voltage of the T waves was noted   The tracing taken on 19/11/42 (Fig 1C) showed a complete return to normal   The patient was seen three months later when she was complaining of headaches   Her heart was normal clinically, radiologically, and cardiographically, but her B P was 170/100 and the retinal vessels were thought to be slightly thickened

Case 8, para 0, aged 21   Admitted on 22/9/44 complaining of headaches, dimness of vision, and eclamptic fits of three days' duration   She was delivered on 25/9/44   The highest blood pressure was recorded on the second post-partum day when it was 180/110   The first cardiogram (Fig 2A), taken on 27/9/44, showed T wave changes and small R wave in lead CR_2 Another taken 7 days later showed improvement (Fig 2B)   Her B P came down to 120/85   The albuminuria and œdema had disappeared, and radioscopic examination showed a normal-sized heart   The patient was seen

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again in March 1945, when her B P was 120/80 and the clinical, radiological, and cardiographic findings were also normal

Case 11, para 10, aged 38   Admitted on 6/10/44 with marked œdema of the legs, albuminuria, and a B P of 200/140   She was delivered on 12/10/44 by Cæsarean section   On 14/10/44 her B P was 160/100 and there was a slight papillœdema   Clinically, the heart was normal   However, a cardiogram taken on the same day (Fig 3A) showed flat T wave in leads II and IVR, and inverted T wave in leads III and CR$_2$, the initial deflection was absent in CR$_2$, and the electrical systole was prolonged Fig 3B, taken on 18/10/44, showed improvement   On 25/10/44 the cardiogram still showed an absent R wave in lead CR$_2$ but otherwise it was normal (Fig 3C)   On radioscopic examination, the heart was normal in size   The optic discs looked normal   There was no œdema and no albuminuria, the B P, however, remained 160/100

Case 13, aged 34   Admitted on 15/12/44 with œdema of legs, albuminuria, and a B P of 160/100 She was delivered on 24/12/44   On 6/1/45 she was found to have tachycardia, triple rhythm, and evidences of pulmonary congestion   The retinal vessels looked normal, and the B P was 150/100

TABLE I

CARDIOVASCULAR FINDINGS IN TOXÆMIA OF PREGNANCY

| Case No	Age	Toxæmia	B P (maximum)	Heart			Electro-cardiogram	Remarks
				Rate	Sounds	Size		
1 (Fig 1)	36	Severe	185/120	140	Triple rhythm	Normal (X-ray)	Inverted TI, TII, TIV	Left ventricular failure
2	29	Mild	160/100	88	Normal	Normal	Normal	—
3	29	Severe eclampsia	170/100	80	Normal	Normal (X-ray)	Low TII In-verted TIII Low TIV	—
4	34	Severe	180/130	60	Normal	Normal	Normal	—
5	25	Severe	190/130	100	Normal	Normal	Normal	—
6	22	Severe eclampsia	130/95	130	Normal	Normal	Normal	—
7	32	Severe	160/110	120	Normal	Normal	Low TI Isoelec-tric TIV	—
8 (Fig 2)	21	Severe eclampsia	180/110	80	Normal	Normal (X-ray)	Isoelectric TI In-verted TIV	—
9	29	Severe	180/110	90	Normal Apical S M	Normal	Depressed S-TIV Low TIV RIV <2 mm	—
10	23	Mild	160/100	70	Normal	Normal	Normal	—
11 (Fig 3)	38	Severe	200/140	110	Normal	Normal (X-ray)	Isoelectric TII Inverted TIII and TIV	?Antecedent hyper-tension Cæsarean section
12	23	Mild	160/100	90	Normal	Normal (X-ray)	Low TIV	?Antecedent hyper-tension Died of uræmia six months later
13	34	Mild	160/100	100	Triple rhythm	LV+ (X-ray)	Normal	Left ventricular failure, ? ante-cedent hyperten-sion
14	36	Mild	150/100	70	Normal	Normal	P–R+	—
15	31	Severe	170/105	80	Normal	Normal	Normal	—
16	32	Severe	175/115	90	Normal	Normal	RIV<2 mm	Delivered by Cæsar-ean section
17 (Fig 4)	21	Severe eclampsia	210/140	130	Normal	Normal (X-ray)	Low TI Invert-ed TIV Extra-systoles	Post-partum vascu-lar collapse
18 (Fig 5)	21	Severe	200/150	100	Normal	Normal (X-ray)	Isoelectric TII Inverted TIII and TIV	—
19	31	Severe	200/110	100	Triple rhythm	Normal (X-ray)	Normal	Left ventricular failure
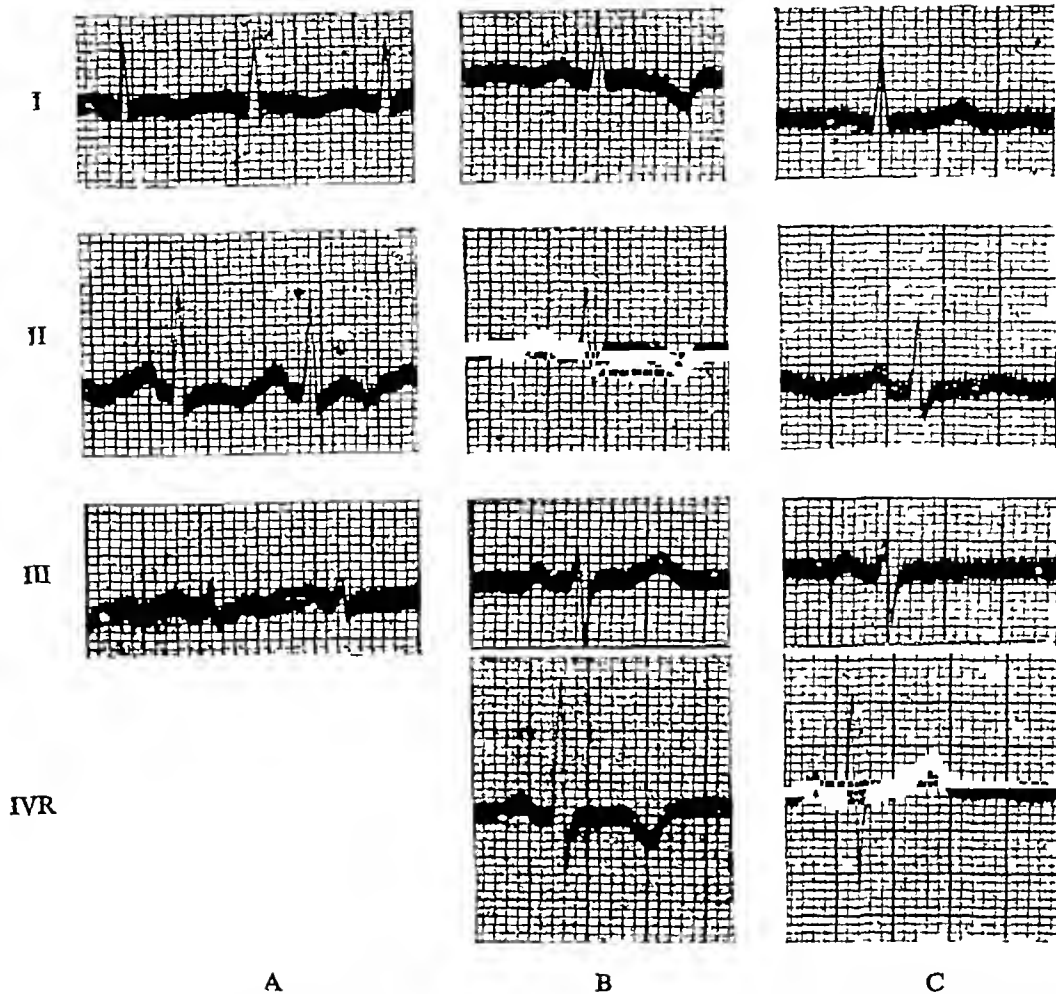
Fig 1 —Case 1   Toxæmia complicated by left ventricular failure   Delivered on 24/7/42
(A) 27/7/42, abnormal T waves   (B) 18/8/42, deeply inverted T wave in leads I II, and IV
(C) 19/11/42, normal tracing

A cardiogram showed left axis deviation and normal complexes   The radioscopic examination showed slight enlargement of the left ventricle   The patient made a good recovery, the triple rhythm and the pulmonary congestion had disappeared   She was discharged and a follow-up was, unfortunately, impossible

Case 17, para 0, aged 21   Admitted on 9/4/46 with eclampsia, albuminuria, and œdema of legs and face   Her B P was 210/140   She was delivered on the same day   Twelve hours after delivery she showed evidences of a vascular collapse, the heart rate being 130 a minute and the B P 90/70 The patient had only a very slight loss of blood, which could not account for the collapse   She was given blood and plasma transfusions and she gradually improved   On 11/4/46 her B P was 130/90 Fig 4A showed flat T II and inverted T in leads III and CR$_2$ There was some improvement in Fig 4B and C, taken five and nine days later

Case 18, para 0, aged 21   Admitted on 12/4/46 with severe albuminuria and œdema of legs   The B P was 200/150, and there was a slight papillœdema   She was delivered on 16/4/46   Fig 5A, taken the next day, showed the T waves flat in leads II and IVR, and inverted in leads III and CR$_2$ Clinically the heart was normal   The B P was 170/145, on the same day and on 23/4/46 had fallen to 150/120   The cardiogram (Fig 5B) showed higher T waves   On 27/4/46 the B P was 130/90 and the optic discs looked normal   The cardiogram showed no abnormality (Fig. 5C), and on screen examination the heart was normal in size   Also the œdema and albuminuria had completely cleared up

Case 19, para 4, aged 31   Admitted on 28/6/46 with severe œdema of the legs   The B P was 200/110   On 2/7/46 she suddenly became very dyspnœic, and was found to have tachycardia with triple rhythm and pulmonary congestion   No cardiogram was done   She was delivered on 6/7/46 Following delivery, there was a gradual improvement, and on 18/7/46 the clinical, cardioscopic, and cardiographic findings were normal   Her B P was 130/80, and the œdema of the legs had cleared up completely   The patient was seen again a month later, when the cardiovascular system was found to be normal in every respect

I

II

III

IVR

CR₂

A   B
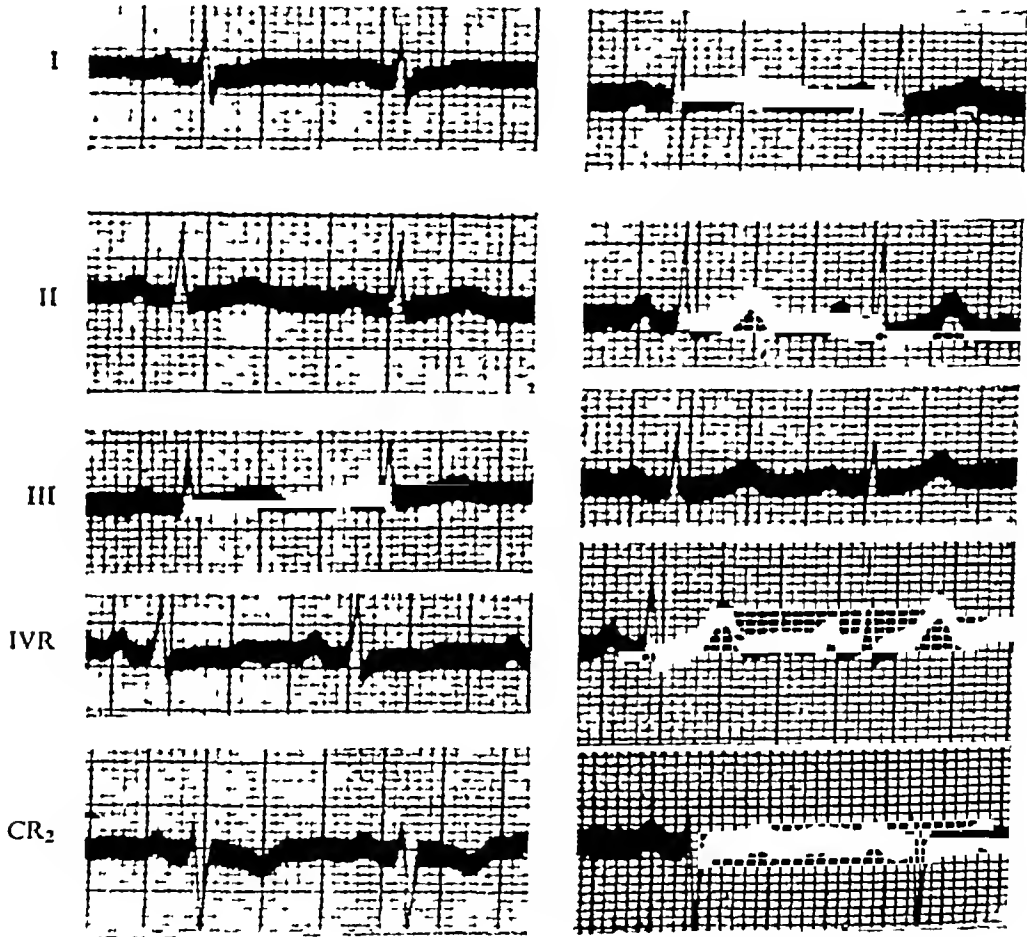
Fig 2 —Case 8   Eclampsia   Delivered on 25/9/44
(A) 27/9/44, flat or inverted T waves   (B) 9/10/44, T waves returning to normal

DISCUSSION

In the present series a total of 7 patients (37 per cent) were thought to have significant changes in the heart   2 showed clinical changes only, 4 cardiographic changes only, and 1 showed both clinical and cardiographic evidence of cardiac involvement   This incidence of cardiac involvement in toxæmia of pregnancy is somewhat lower than that recently reported by Wallace *et al* (1946), who found cardiac changes in 6 of 12 cases

Thomson, Cohen, and Hamilton (1938) observed transient abnormality of the T wave in the chest lead in some of their normal pregnant patients   Wallace *et al* (1946), found an inverted T wave in lead CF₂ in a pregnant woman whose heart was believed to be normal, and suggested that such inversion of T in the chest lead may occur in normal pregnancy

As regards our present series, we believe that the cardiographic changes were indicative of myocardial damage in at least 5 cases, because they occurred in both standard and chest leads, and persisted for some time after delivery, so that the alteration in the anatomical position of the heart during pregnancy could be excluded as causative factors   Furthermore, one of us (P S) has examined the records of several pregnant women, including patients with normal hearts, with chronic rheumatic heart disease, and with permanent arterial hypertension

	A	B	C
I			
II			
III			
IVR			
CR₃			
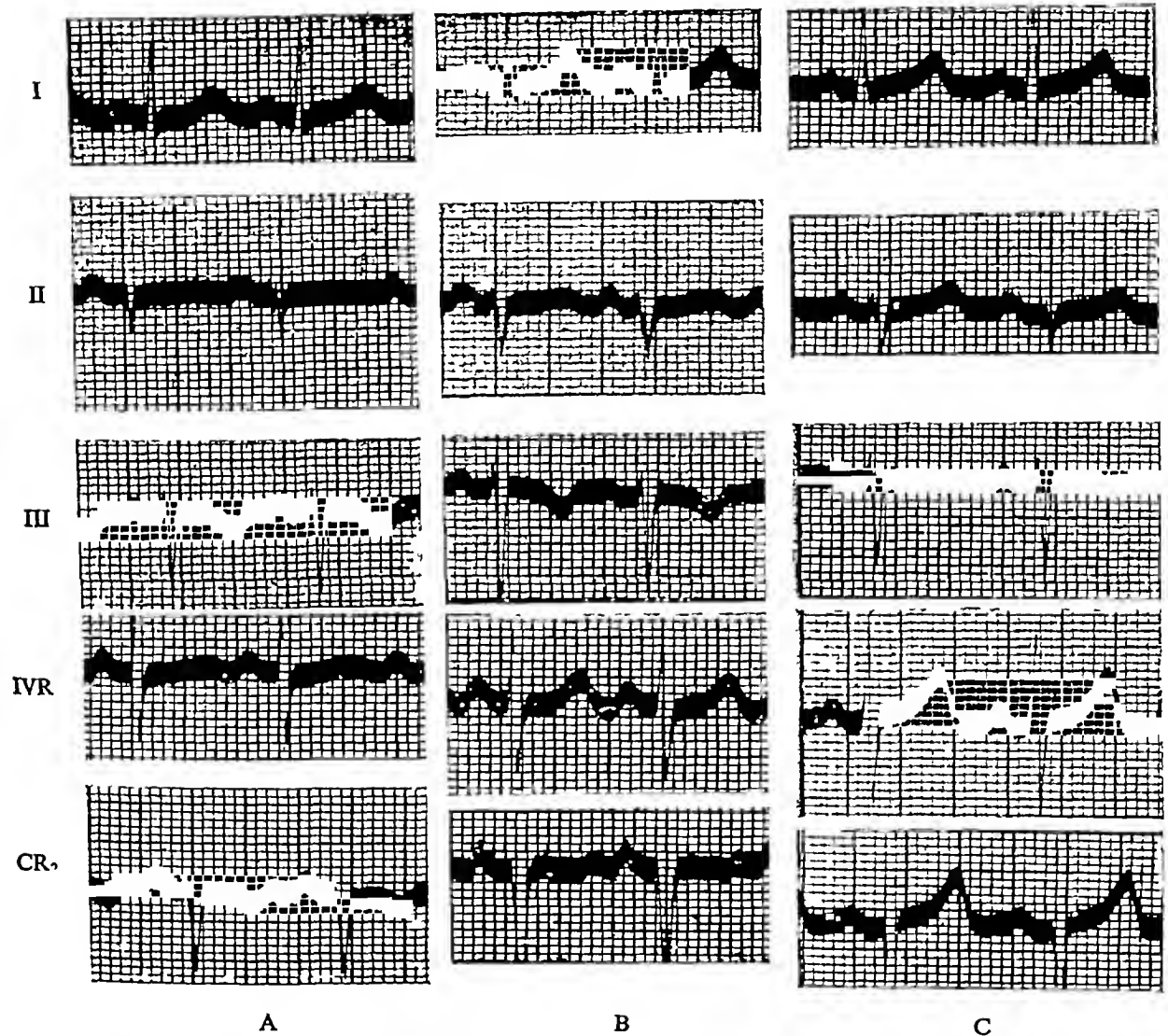
FIG 3 —Case 11   Probable chronic hypertension with superimposed toxæmia.   Delivered by Cæsarean section on 12/10/44
(A) 14/10/44, definite T wave changes, absent R wave in CR₂, prolonged electrical systole.   (B) 18/10/44, T waves getting higher   (C) 25/10/44, still absent R wave in CR₂, otherwise normal tracing.

without superimposed toxæmia, both ante-partum and post-partum, and has not observed a sequence of cardiographic changes similar to those seen in some of the toxæmic patients

The changes in the heart appear to be temporary, but their duration varies considerably The changes may not only persist for some time after delivery, but may become greater in the post-partum period   This has been previously stressed by Dexter and Weiss (1941) and Wallace et al (1946), and is also borne out by our own observations

Although it is highly probable that there is a causal relationship between toxæmia of pregnancy and cardiac damage, it is not quite clear how the latter is brought about   According to Dexter and Weiss (1941) the syndrome of cardiac asthma and pulmonary œdema may be caused by two factors, singly or combined—primary fluid retention in the lung tissue caused by factors specific to toxæmia, and left ventricular failure—and the mechanism of pulmonary
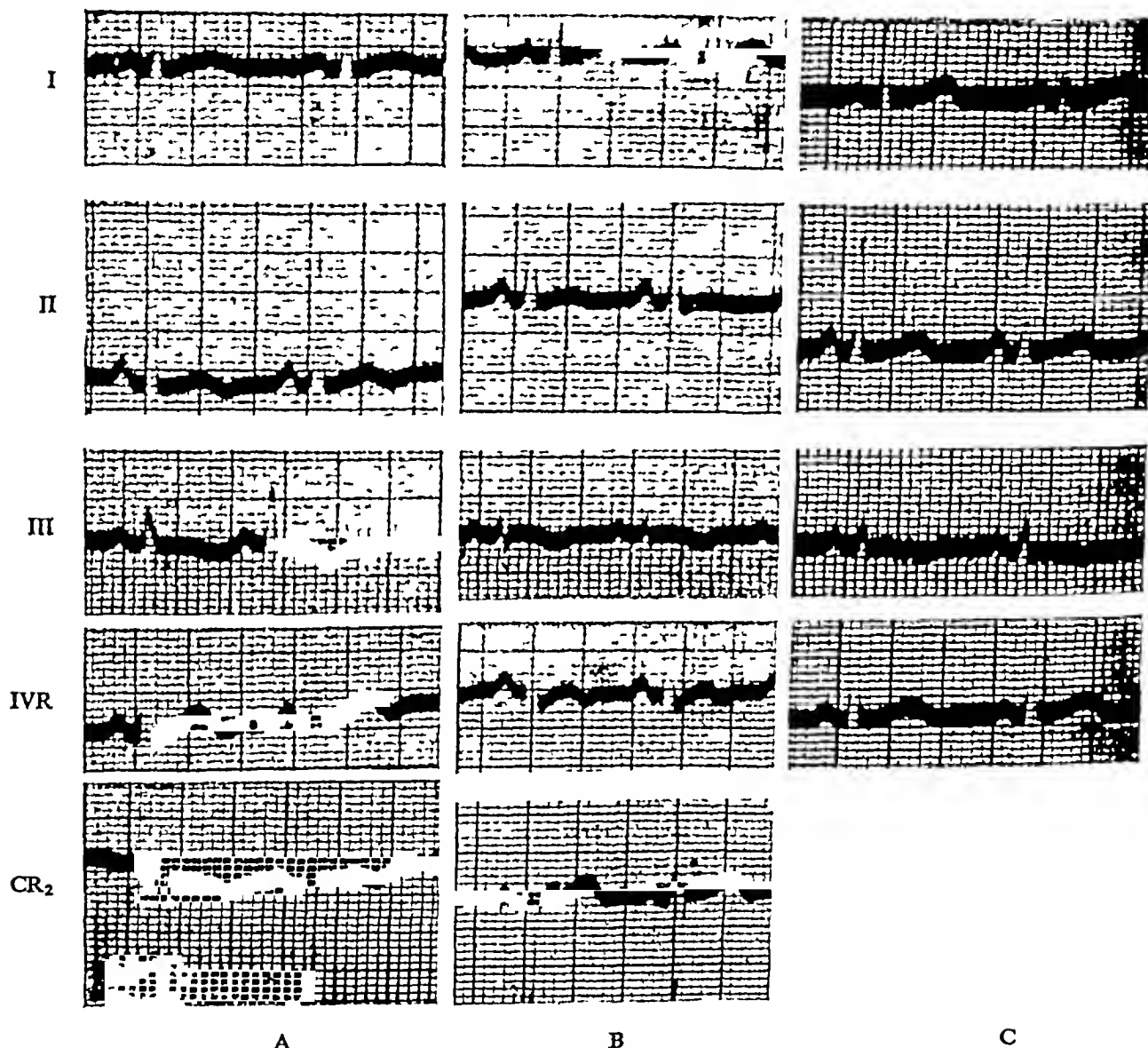
FIG 4 —Case 17   Eclampsia   Delivered on 9/4/46   Post-partum vascular collapse.
(A) 11/4/46, T wave changes, extrasystole in lead III.   (B) 16/4/46, T in CR₂ positive, but still abnormal tracing.   (C) 20/4/46, T waves returning to normal.

œdema in toxæmia of pregnancy is in many respects similar to that in beri-beri   Although there are some reports suggesting a causal relationship between toxæmia of pregnancy and vitamin B_1 deficiency (Siddall, 1940, King and Ride, 1945), the clinical and especially the cardiographic features of myocardial injury in toxæmia are unlike those seen in beri-beri heart disease

Dieckmann (1942) found that in pre-eclampsia especially if severe, there is a concentration of blood during the height of the disease and dilution with clinical improvement.   According

to him hæmo-concentration places a tremendous strain on the heart because the thickened blood with increased viscosity requires more work by the heart and at the same time favours a decrease in the coronary circulation   Wallace *et al.* (1946) are of the opinion that focal myocardial necrosis, œdema, and infiltration are the essential factors in producing the cardiographic changes and precipitating the heart failure

While the cardiac failure of the left ventricular type may be in some cases the direct result of the hypertension, it is unlikely that the latter condition is responsible for the cardiographic
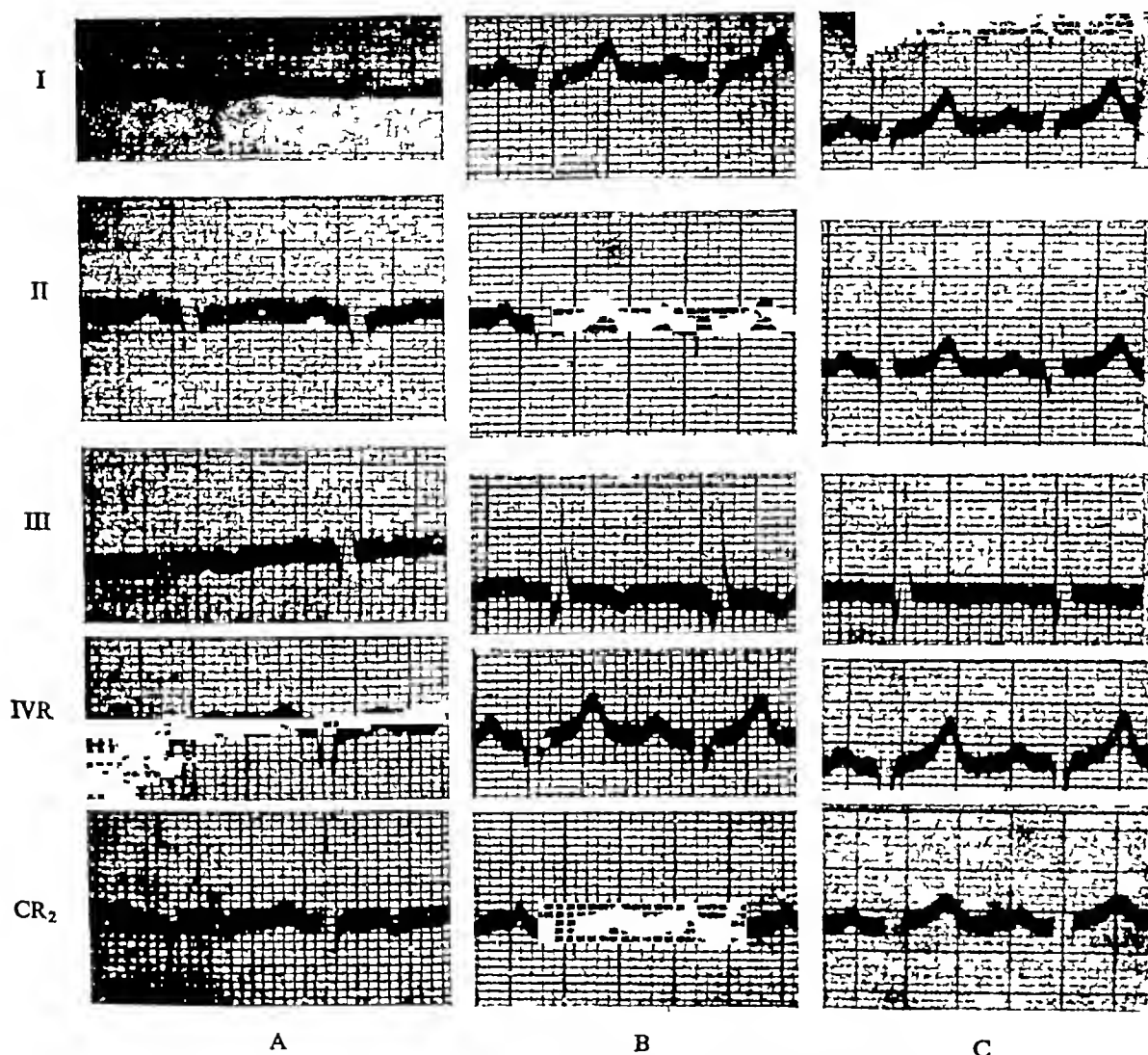
FIG 5 —Case 18   Severe toxæmia   Delivered on 16/4/46
(A) 17/4/46, marked T wave changes   (B) 23/4/46, T waves getting higher   (C) 27/4/46, normal tracing

changes   The rise in the blood pressure in pure toxæmia or in patients with antecedent hypertension and superimposed toxæmia is usually not of sufficient duration to be an ætiological factor   On the other hand, the changes, if any, in persistent hypertension would not be limited to the period of pregnancy and the puerperium   One can assume, therefore, that the cardiographic abnormalities indicate changes in the heart that have a direct bearing on the " toxæmic " state   We have recently had the opportunity of following up a 28-year-old primigravida who had coarctation of the aorta with a blood pressure of 220/130 in the upper

extremities and enlargement of the left ventricle   There was nothing to suggest a superimposed toxæmia   Frequent cardiograms were done, including IVR and CR_2 chest leads, from early pregnancy to the puerperium, and all records were strictly normal

It would appear from our observations that gross cardiac enlargement is not a feature of pure " toxæmic " cardiac lesion, irrespective of the presence or absence of cardiac failure   Only one of our cases (Case 13) showed enlargement of the left ventricle   It is true that the radioscopic examination in many of our cases was not carried out at the height of the disease, nevertheless, the clinical impression as a rule was that of a normal-sized heart   If gross cardiac enlargement is present, it probably indicates either antecedent hypertension or heart disease not " toxæmic " in origin   There is nothing to suggest that pericardial effusion is present in toxæmia of pregnancy to account for the cardiographic changes or the heart failure

Toxæmia of pregnancy is an acute vascular disorder and in this respect it closely resembles acute glomerulo-nephritis (Dexter and Weiss, 1941)   Cardiac involvement is known to occur in acute nephritis   Ellis (1942) found cardiac impairment in 21 per cent of his cases of acute nephritis, and states that " the picture is that of the left ventricular failure with pulmonary œdema, it is possibly due to involvement of the myocardial vessels in the widespread vascular disorder that we believe to be characteristic of this type of nephritis "   Cardiographic changes may also be present in acute nephritis (Langendorf and Pick, 1938), and Wallace et al (1946) pointed out recently that the cardiographic changes observed in toxæmia of pregnancy are similar to those seen occasionally in acute glomerulo-nephritis   Our as yet unpublished observations are in agreement with this view   Wallace et al (1946), however, are inclined to think that while the predominant pathological changes in the heart in acute nephritis result from vascular damage, the changes in toxæmia of pregnancy consist of focal myocardial necrosis   This is supported to a great extent by the available pathological findings (Teel, Reid, and Hertig, 1937, Gouley, McMillan, and Bellett, 1937)   On the other hand, it is now well established, both clinically and anatomically, that toxæmia of pregnancy is associated with generalized vascular changes (Bell, 1932, Wagener, 1933, Herrick and Tillman, 1935, Jones, 1937, and Browne, 1944)   Wagener (1933) states that in "toxæmia of pregnancy —just as in glomerulo-nephritis—the presence of lesions of the retinal arteries is an indication of involvement of the systemic and renal arterioles of similar type and severity "   According to Browne (1944) arteriolar spasm can be seen in the arterioles of the retina in pre-eclamptic toxæmia when the blood pressure exceeds 150   Bell (1932) showed that in fatal cases of eclampsia there was a narrowing of all the glomerular capillaries   Herrick and Tillman (1935) found widespread vascular changes in the arteries of the kidneys, spleen, pancreas, suprarenal glands, and liver   Teel et al (1937) found, in addition to œdema and leucocytic infiltration of the myocardium, also minor changes in the small coronary vessels

Although convincing proof is still lacking of a direct damage to the myocardial vessels in toxæmia of pregnancy, in the light of the above-mentioned clinical and anatomical findings the possibility of structural damage to the small coronary branches cannot be excluded with certainty   There appeared to be no close correlation between the severity of the toxæmic state and the degree of cardiac damage   The duration of the toxæmia may be more important than its severity in producing the cardiac damage

The true significance of the observations presented in this paper lies in showing that cardiac involvement is not uncommon in toxæmia of pregnancy   We believe that some of the cases of acute ante-partum or post-partum cardiac failure of undetermined ætiology may be instances of toxæmia, even if the recognized signs of the latter condition are not convincingly present at the time of the onset of the cardiac failure, and that some of the cases of vascular collapse known as " obstetric shock " may be instances of true toxæmia   The clinical picture of post-partum vascular collapse in one of our cases (Case 17) was identical with that of so-called " obstetric shock "   Most such cases are associated with traumatic delivery and post-partum

loss, and the chief causative factor is blood loss   There remain, however, those infrequent but important cases where collapse occurs with minimal loss after normal labour and delivery, our Case 17 being an example   Such cases may be instances of toxæmia of pregnancy with associated myocardial damage

SUMMARY AND CONCLUSIONS

The heart was studied in 19 unselected cases of toxæmia of pregnancy   Clinical and cardiographic examinations were made in all of them, and 9 were also studied radiologically

Seven patients showed significant cardiac involvement   One developed left ventricular failure, with T wave changes in the cardiogram similar to those seen in anterior myocardial infarction   Two had left ventricular failure with normal cardiographic tracings   Four others showed no clinical evidence of cardiac failure, but their cardiograms showed T wave changes that were interpreted as indicating myocardial damage, and one of these developed post-partum vascular collapse   Six patients showed cardiographic changes of doubtful significance, and in six both the clinical and the cardiographic findings were perfectly normal

The clinical and cardiographic manifestations were of a transient nature   Cardiac enlargement was found in only one case, and the belief is expressed that gross cardiac enlargement is not a feature of pure " toxæmic " cardiac lesion irrespective of the presence or absence of cardiac failure

The pathogenesis of the cardiac lesion is discussed, and it is suggested that either direct vascular damage—as in acute glomerulo-nephritis—or primary focal myocardial necrosis, or both, have to be considered

Cardiac involvement is not an uncommon complication of toxæmia of pregnancy, and some of the unusual types of heart failure occurring in late pregnancy and in the early puerperium, and also some of the cases of post-partum vascular collapse may be instances of toxæmia of pregnancy with associated myocardial damage

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ABSTRACTS OF CARDIOLOGY

A Study of Abnormal T Waves in Patients presenting No Evidence of Organic Heart Disease I STEIN *J Lab clin Med*, 31, 837–849, Aug, 1946

With wider use of electrocardiographs it is increasingly important that minor deviations should not be taken for evidence of heart disease, and that the limits of the normal should be widely recognized Stein has studied 4810 soldiers at an Army hospital who were considered free from heart disease Most were men between 20 and 40 More than 1 per cent (51) showed T wave changes that might be thought pathological, 23 predominantly in CR4 and 28 in the standard limb leads More than half of these were psychoneurotic, and none had any other evidence of heart disease after full examination, including cardioscopy Forty-three of 50 patients with T wave changes had normal upright T waves after exercise

When Graybiel and White first drew attention to the possibility of T II inversion without heart disease it was mainly in patients with neuro-circulatory asthenia, though the importance of posture and a high diaphragm was also stressed The authors did not think that fear or emotion resulting from the examination was the responsible factor, but rather attributed the changes to autonomic nervous imbalance They stress the importance of not making a mistaken diagnosis of heart disease
Maurice Campbell

The Influence of Age on Blood Pressure A Study of 5,331 White Male Subjects H I RUSSEK, M M RATH, B L ZOHMAN, and I MILLER *Amer Heart J*, 32, 468–479, Oct, 1946

A statistical analysis of the systolic and diastolic blood pressure readings of 5331 white males between the ages of 40 and 95 years is presented The subjects were observed in two service hospitals and two institutions for aged people The gist of the findings is that a systolic blood pressure below " 100 plus the age " is " normal," and a diastolic blood pressure of over 90 mm Hg is abnormal at any age
H E Holling

Magnesium Sulfate in Paroxysmal Tachycardia W T ZIMDAHL *Ann intern Med*, 25, 531–533, Sept, 1946

An attack of paroxysmal auricular tachycardia, which responded to intravenous magnesium sulphate, is described Carotid sinus pressure, ocular pressure, quinidine sulphate (3 gr (0 2 g) intravenously every 2 hours for 12 hours), rapid digitalization with lanatocide-C, 0 8 mg intravenously followed by 0 1 g of

digitalis leaf every 4 hours, and mecholyl (acetyl β-methylcholine chloride) 25 mg subcutaneously, were all tried without effect As the patient's condition was so poor it was considered advisable to stop the arrhythmia if possible, and he was given 10 ml of 25% magnesium sulphate solution intravenously, This, too, had no effect, so 6 hours later he was given 22 ml of 25% magnesium sulphate solution intravenously and the attack ceased while the needle was still in the vein This dosage is somewhat higher than that usually recommended of 10 to 20 ml of 20% solution
S Oram

Effect of 1262 Γ (" Dacorene ") on Recurrent Paroxysmal Tachycardia R FROMENT and L GALLARVADIN *J Méd Lyon*, 27, 725–726, Oct 20, 1946

" Dacorene " (diethyl-aminoethoxy-2-diphenyl chlorhydrate) is a synthetic sympathetic inhibitor said to act predominantly on the heart The authors report the results of its administration in 2 cases—one of supraventricular paroxysmal tachycardia and one of auricular flutter [No electrocardiograms are reproduced] The first patient, a man of 53, had had attacks of tachycardia since the age of 6, after the age of 46 they became more frequent and of longer duration With quinidine 9 gr (0 6 g) thrice daily the frequency of the attacks was reduced, but the drug gave rise to toxic symptoms The dose was reduced and on the whole the frequency of the attacks continued to diminish, though varying from time to time Dacorene was combined with the quinidine, and then the two drugs were given alternately The attacks gradually became less, and of about the same frequency with either drug The dacorene had no toxic effects In the second case, that of a man of 64, there were attacks of auricular flutter with 1-to-1 response or 2-to-1 or a higher degree of block Quinidine was without effect on these paroxysms,' but dacorene (150 mg 4 times daily) suppressed them while the patient was in hospital He continued this dosage for a month after his discharge and remained free of attacks Then he took smaller and irregular doses and noted a recurrence of the paroxysms Indications for its use, dosage, and mode of action have still to be worked out
S H Cookson

The Conducting System of the Vertebrate Heart F DAVIES and E T B FRANCIS *Biological Reviews*, 21, 173–188, Oct, 1946

A brief review is given of the most important work on the structures responsible for the initiation and conduction of the impulse to contraction in the vertebrate

heart The authors conclude that in fish, amphibia, and reptiles the cardiac muscle fibres form a continuum with the same general histological characters in all parts of the heart Since there is no structural specificity of the muscle fibres, factors other than purely morphological ones must account for the different intrinsic rhythms displayed by the individual heart chambers They suggest, on the basis of unpublished work, that a differential distribution between auricle and ventricle of certain chemical substances (glycogen, phosphocreatine, and adenosine compounds), known to be concerned with muscular contraction, may have a bearing on this problem

In birds and mammals, specialized tissue (the nodes, A-V bundle, and Purkinje fibres) has been developed to initiate and conduct the impulse to contraction The structure and distribution of these specialized fibres are in general the same for birds and mammals There are, however, certain differences which the authors hold may be related to the different functional requirements of the hearts Collateral evidence is brought to support the view that the specialized tissues of the avian and mammalian heart are not remnants of more extensive tissues of a similar nature in lower vertebrate hearts, but are new developments associated with the more rapid heart rate in the higher vertebrates
R T Grant

Complete Heart Block in Pregnancy T J QUINTIN *Canad med Ass J* , 55, 600–601, Dec , 1946

Complete heart block is a rarity among pregnant women, 14 cases only having been recorded up to 1938 The author describes a patient who had two normal pregnancies and confinements Symptoms were negligible except for slight dyspnœa on exertion during the last 2 months before the second confinement and some giddiness after stooping Laboratory investigations did not reveal the cause of the heart block *Braithwaite Rickford*

Prognostic Significance of the Diastolic Blood Pressure in Eclampsia Patients L VÁCZY *Gynaecologia*, 122, 244–251, Oct , 1946

It is difficult to decide whether the course of an eclamptic case will be mild or severe Various investigations, such as estimation of the histamine content of the urine, measurement of capillary pressure in the skin or of muscle tone, and liver function tests, have been suggested in the past but are of little use at the bedside This paper shows the value of blood pressure readings in prognosis during the acute stage of eclampsia The systolic, pulse, and diastolic pressure readings in 24 cases are discussed

No prognostic significance could be attached to the systolic blood pressure Thus, 12 of the 24 patients had an average systolic blood pressure of over 180 mm and had only 3 fits, while 12 with an average of 178 mm had more than 3 fits Further, 7 women who had only 1 fit had a systolic pressure of over 200 mm while 6 who had 5 fits had one of less than 200 mm

The pulse pressure was also of no prognostic value Patients with a diastolic pressure of over 100 mm generally had more fits than those with a diastolic pressure below 100 There was no absolute connection between the height of the diastolic pressure and the number of fits, but it could be said that when the diastolic pressure was below 100 mm the prognosis was better than when it was above 100 *Gladys Dodds*

Atherosclerotic Valvular Disease of the Heart C T ASHWORTH *Arch Path* , 42, 285–298, Sept , 1946

The author found atherosclerotic valvular disease of the heart recorded in 101 of 500 consecutive necropsies and himself found changes of some degree in 63% of hearts carefully examined The lesions were moderate or severe in 7% of the 500 necropsies The mitral valve was usually the first to be affected, but in most cases both it and the aortic valve were involved The tricuspid and pulmonary valves always escaped The earliest lesion was an atheromatous one on the " outflow " surface of the valve—that is, the aortic surface of the aortic valve, and the ventricular surface of the mitral valve Diffuse thickening or sclerosis followed, often with the deposition of calcareous plaques The more extreme lesions of the aortic valve caused stenosis and insufficiency The anterior cusp of the mitral valve was more commonly and more intensely involved than the posterior, calcification, stenosis, and incompetence were all rarer than in the aortic valve In 10 hearts the annulus fibrosus of the mitral valve was occupied by a more or less complete ring of calcification, two of these cases had had complete heart block

The frequency and severity of the lesions increased with age, and changes of some degree were nearly always present in subjects over 50 years Incidence was not related to sex or race, nor was valvular sclerosis related to hypertension The disease was not often clinically manifest, and only the more severe lesions caused cardiac murmurs The more extreme degrees of calcification sometimes contributed to death by aortic stenosis or by heart-block due to calcification of the annulus fibrosus of the mitral valve The degree of valvular atherosclerosis was similar to that in the upper aorta and coronary arteries The ætiology of the condition would appear to be the same as that of atherosclerosis elsewhere, with the additional factors that the affected parts of the valves are the least cellular and vascular, and the most subject to tension and vibration *Martin Hynes*

The Relation between Circulation Time and the Amount of the Residual Blood of the Heart. B GERNANDT and G NYLIN *Amer Heart J* , 32, 411–418, Oct , 1946

The authors have measured the " circulation time," the " heart volume," and the brachial venous pressure in 308 patients with heart disease In 214 of the patients the heart lesion was compensated and

in 94 it was decompensated, as evidence by œdema, a palpable liver and spleen, and pulmonary congestion

They find in all cases a significant relation between the heart volume and the circulation time They also state that " the studies have clearly proved that, above all, the circulation time depends on the amount of residual blood in the heart and only to a slight extent on the degree of decompensation, i e , of congestion "

Correlation	Number	$r \pm \sigma r$
Volume (V/M²)-circulation time	93	0 37±0 090
Volume (V/M²)-venous pressure	93	0 37±0 090
Venous pressure-circulation time	94	0 39±0 088

[This last statement does not seem to be borne out by the correlation coefficients given for relative heart volume, circulation time, and degree of decompensation (as measured by the venous pressure) as shown in the table] *H Γ Holling*

Cardiac Output in Heart Failure J R E SUAREZ, J C FASCIOLO, and A C TAQUINI *Amer Heart J*, 32, 339–356, Sept , 1946

This is a study of 42 patients with different types of valvular, hypertensive, or coronary heart disease, and of 17 normal subjects The cardiac patients were graded into 4 classes according to the criteria of the New York Heart Association (1) patients with no limitation of physical activity, (2) those with slight limitation of physical activity, (3) those with marked limitation, and (4) those who are unable to carry on any physical activity without discomfort Grollman's acetylene method was used, 4 samples being taken The results were subjected to statistical analysis, and are shown in the table

	Normal	Class 1	Class 2	Class 3	Class 4
Cardiac index in litres per sq metre per minute	2 27 ±0 06	2 35 ±0 19	2 03 ±0 05	1 73 ±0 09	1 58
Arterio-venous oxygen difference in ml per litre of blood	60 4 ±1 78	62 2 ±6 53	66 9 ±1 85	81 0 ±3 96	91 8
Systolic output in ml per sq metre of body surface	35 4 ±0 76	35 3 ±2 81	29 8 ±1 14	23 8 ±1 29	19 3
Pulse rate Mitral disease	63	63	70	83	98
Other diseases		74	66	71	77

Classes 3 and 4 represent failure

The authors conclude that there is an inverse correlation between the degree of cardiac failure and the cardiac output, and a direct correlation between the degree of failure and increase in the arterio-venous oxygen difference Systolic output goes down as failure increases in degree In mitral cases the pulse rate rises as failure advances, but in other forms of heart disease behaviour of the rate is rather irregular
James W Brown

Myocardial Lesions due to Starvation R FORSTER *Cardiologia* , 10, 369–378, 1946

This paper describes the clinical and post-mortem changes in 31 cases of starvation from German concentration camps The most frequent electro-cardiographic finding was a reduction in amplitude of the deflections, particularly of the T wave At necropsy the most frequent cardiac change found was fatty degeneration of the myocardium In these cases recognizable vitamin deficiencies were seldom seen, though infections and pre-existing cardiac abnormalities were frequent The mechanism of the changes seen is discussed *H E Holling*

The T Wave of the Precordial Electrocardiogram at Different Age Levels R M SUAREZ and R M SUAREZ, JR *Amer Heart J* , 32, 480–493, Oct , 1946

Inverted T waves occur in the præcordial electro-cardiograms of normal subjects up to 15 years of age The present observations were made to determine the incidence of these findings in various age groups in 161 healthy Puerto Ricans, aged 5 to 46 years With the exploring electrode paired with the arm and leg leads through a central terminal, records were taken from the six classical chest positions (C V 1 to C V 6) In the youngest subjects up to 12 years old, inverted or diphasic T waves were found as far laterally as position 5, in subjects 12 to 18 years of age as far as position 4, and in adults as far as position 3 The results suggest that, irrespective of age or sex, a negative T wave in C V 6 may be regarded as abnormal while the same finding in C V 1 may be normal Negative T waves in C V 4 or C V 5 are probably abnormal over 12 years of age
W J H Butterfield

The Heart in Rheumatoid Arthritis A S ROGEN *Brit med J* , 1, 87–88, Jan 18, 1947

The author reviews recent work on the ætiological relationships between rheumatic fever and rheumatoid arthritis, with special reference to the cardiovascular system in 33 consecutive cases of rheumatoid arthritis, 22 of which were females Careful search was made for evidence of mitral stenosis but none was found In 1 case only, a woman of 68, was there a loud apical systolic bruit which was considered to be organic, in 8 cases there was a functional murmur The electrocardiograms of 29 patients showed no changes that could be held to be suggestive of rheumatic fever, though in some cases there were T wave

changes corresponding in all probability to the state of arterial degeneration occurring in old people, who formed the majority of the patients in this series No macroscopical or histological changes of rheumatic fever were seen in the 1 case that came to necropsy

These results are at variance with the reports of some, but not all, workers, and serve to emphasize the limited value of comparisons between the clinical manifestations of rheumatic fever and rheumatoid arthritis in the present state of our knowledge of the rheumatic diseases   *J W Brown*

A Refractory Case of Subacute Bacterial Endocarditis due to *Veillonella gazogenes* clinically Arrested by a combination of Penicillin, Sodium para-Amino-hippurate and Heparin L LOEWE, P ROSENBLATT, and E ALTUREWERBER *Amer Heart J* , 32, 327–338, Sept., 1946

The unique case is described of a 35-year-old man who suffered from subacute bacterial endocarditis due to *Veillonella gazogenes*, a Gram-negative anærobic coccus During a year of treatment he received about 467,000,000 units of penicillin, and, at the end of that time, although his blood culture was still positive and his subacute endocarditis active, he was felt not to have deteriorated much *In vitro* tests showed bacteriostasis at 10 units of penicillin per ml , and that 30 units per ml were required for a complete bactericidal effect Previous studies had shown that a blood level of 1 unit per ml could be expected for each million units of penicillin administered daily Thus to reach the desired level 30,000,000 units a day was necessary It was therefore decided to use *p*-aminohippuric acid as an enhancing agent Treatment was accordingly started by the intravenous route with the daily administration of 10,000,000 units of penicillin dissolved in 2 litres of 12 per cent sodium *p*-aminohippurate solution to which was added 50 mg of heparin The heparin was used to prevent thrombophlebitis at the site of injection This mixture produced prompt results, and within 3 days the temperature became normal, and has remained so for 6 months The treatment was continued for 13 days, so that the patient received a total of 130,000,000 units of penicillin   *James W Brown*

Acute Myocardial Infarction in Men Below Forty F STEIGMANN and F CLASSNER *Mil Surg* , 99, 177–181, Sept , 1946

The authors describe acute myocardial infarction in 3 patients, aged 28, 32, and 34, in a naval hospital Observations during the war make it necessary to adjust ideas as to incidence and causative factors Only recently have reports appeared of patients below 40 suffering from coronary thrombosis—a diagnosis which now has to be considered in patients with severe substernal or præcordial pain, be their age 20 or 60 War experience emphasizes effort as precipitating an attack Without implying that this condition cannot occur while at rest in bed, it is noted that in one series 50 per cent followed effort, and only 10 per cent occurred during sleep

Kahn tests were negative in all 3 patients The pneumonitis in the first 2 patients was regarded as contributory Effort played a part in all 3 Electrocardiographic changes are delayed, showing the importance of serial examinations

Failure to recognize effort as a cause, and the possibility of the occurrence of the disease in younger people, might have catastrophic effects The authors consider that arteriosclerosis of the coronaries may occur in young individuals and that effort, cold, and over-eating may bring on acute myocardial infarction with or without associated thrombosis of the coronary vessels   *W N. Pickles*

Bacterial Endocarditis of the Tricuspid Valve. L KAROTKIN and P MARCUSE *South med J* , 39, 769–774, Oct , 1946

The authors draw attention to the difficulty of diagnosing bacterial endocarditis involving only the right side of the heart, signs of organic heart disease are often lacking, the blood culture usually remains negative, and systemic embolism fails to appear unless tissue breakdown occurs in the lungs They report 3 cases of bacterial endocarditis of the tricuspid valve, giving necropsy findings in each case Case 1 had a tricuspid valve already damaged by rheumatism, early blood culture was negative, but later pneumococcus Type VII was grown from venous blood. In Case 2 the endocarditis complicated lobar pneumonia, and the sputum contained Type VII pneumococcus, blood culture was not performed. In Case 3 the valvular lesion occurred in the course of a *Staphylococcus aureus* septicæmia, and blood culture was repeatedly positive Acute bacterial endocarditis of the tricuspid valve alone is rare, and subacute bacterial endocarditis of this valve is even more rare On the other hand, involvement of the tricuspid valve in addition to other valves is " perhaps not quite so rare as is commonly believed " *D Black*

Study of the Electrocardiogram in Auriculo-Ventricular Block (Étude de l'électrocardiogramme dans le bloc atrio-ventriculaire) G FATZER *Cardiologia, Basel*, 10, 305–368, 1946

Forty-four cases of total A–V block were studied (19 men, 25 women) Arteriosclerosis and rheumatic myocarditis were the main causes Arteriosclerosis is more liable to produce intermittent block than myocarditis The prognosis of A–V block depends on the condition of the myocardium, the frequency of Adams-Stokes attacks which carry a bad prognosis, the presence of bundle-branch block, and the length of the Q–T interval Sinus arrhythmia, blood pressure, hæmoglobin values, cardiac enlargement (observed in most cases), and decompensation (in 50 per cent of the cases) were studied in detail   *H E Holling*

Coronary Sinus Rhythm D SCHRF and R HARRIS
Amer Heart J, 32, 443-456, Oct , 1946

In the course of 23 610 routine electrocardıne examına
tions 31 cases of coronary sınus rhythm were diag
nosed on the criterıa of low positive or absent P waves
in lead I, deep, inverted, and usually peaked P waves
in leads II and III and a normal or slightly shortened
P-R interval These changes were previously
observed by Scherf in dogs after warming the coronary
sınus *ın sıtu* The cases were evenly distributed
between the sexes, and the mıjorıty of patients showed
evidence of heart disease The rhythm was very
labile and changed spontaneously or after exercıse,
amyl nıtrıte ınhılatıons or carotid sınus pressure
As the authors point out, it should be noted that, in
our present state of knowledge, it is not possible to
differentiate between rhythms orıgınatıng in the
region of the coronary sınus and in the upper part of
the auriculo ventricular node *W J H Butterfield*

**Abnormalities of the Respiratory Pattern in Patients
with Cardiac Dyspnea** H E HRYN *Amer Heart
J*, 32, 457-467, Oct , 1946

The movements of the chest wall during respiration
were recorded from a Marcy pneumograph on to a
kymograph drum In this way the " respiratory
pattern " was studied in 5 normal subjects, 11 cases
of cardıac dısease wıth clınıcal pulmonary congestion,
and in 2 cases of allergic asthma during the attacks
In the last two groups of subjects the tracings con-
firmed the presence of a prolongation of expiration
and showed a termınal slowıng in this phase After
exercise these cases did not show the relatıve shorten-
ıng of expiration, as compared with ınspıratıon,
which was seen in the normal subjects However,
after receiving 0 5 g amınophyllıne ıntravenously,
5 out of 6 cases of pulmonary congestion and both
cases of asthma showed faster breathing presumed
to be of central origin, with greatly ıncreased vıtal
capacity and shortenıng of the expiratory phase
wıthout termınal slowıng, whıch in the author's
opınıon is due to the relaxation of bronchospasm
W J H Butterfield

Diet Low in Salt (Sodium) in Congestive Heart Failure
E O WHEELER, W C BRIDGES, and P D WHITE
J Amer med Ass, 133, 16-20, Jan 4, 1947

One of the most ımportant changes associated wıth
heart faılure is an ıncrease in volume of the cırculatıng
blood This tends to be particularly distrıbuted in the
venous cırculatıon and seems to be associated wıth a
rise in venous pressure There is no doubt that in
many cases of heart faılure retention of sodium by the
kıdney occurs quıte early Thıs is associated wıth an
ıncrease in the patient's weight, probably due to
ıncrease in the extracellular tissue fluıd There is
parı passu with the retention of sodium a retention of
water Thıs state of affaırs soon leads to the develop-
ment of œdema It would appear that œdema can

be precıpıtated by feedıng sodıum chloride to patients
who have a mıld degree of heart failure

The treatment of œdema has been developed with
particular attention to the reduction of sodium in
the diet If a diet low in sodıum is given, it is
possible to allow a fluıd ıntake dıctated by the
patient's taste The average diet, without salt added
at table, contaıns about 4 to 7 g of sodium chloride,
without salt added in cookıng, it contains 3 to 4 g ,
a low sodıum diet contaıns 1 5 to 2 g of sodıum
chloride No drugs containing sodium should be
gıven On this diet, with the help of occasional
mercurial dıuretıcs or even without them, a patient
can become free from œdema and remaın so The
dısadvantage is in the tasteless food *Terence East*

**Some Observatıons on the Pathogenesis of Edema in
Cardıac Faılure** F RFICHSMAN and H GRANT
Amer Heart J, 32, 438-442, Oct , 1946

Observations were made on 3 patients wıth rheumatic
heart disease and aurıcular fıbrıllatıon, treated wıth
digitalıs All 3 patients had had repeated attacks of
cardıac faılure, in 2 of them associated wıth œdema
When in hospıtal on a diet contaınıng about 3 to 4 g
of sodium chloride the digitalıs was wıthdrawn, and
the venous pressure (measured directly) in these
patients rose before there was formation of œdema
E B Reeve

**The Rationale for the Treatment of Angına Pectoris by
Irradıatıon of the Adrenal Glands** W C FISHER
and R L McMILLAN *N C med J*, 7, 547-550,
Oct , 1946

Experimental evidence from the lıterature is selected
to lend support to the view that angina pectoris is due
to dıscharges of adrenaline, which ıncrease the cardıac
demand for oxygen, coupled with ınabılıty of athero-
sclerotic coronary arteries to dilate proportionately
Thus the heart of a dog acted on by adrenaline may
consume four tımes the normal amount of oxygen
The four most common precıpıtatıng causes of angına
—effort, emotion, over-eatıng, and cold—have been
shown to provoke an adrenalıne dıscharge A sub-
cutaneous ınjection of 0 5 to 1 mg of adrenaline is
known to ınduce an attack of angına pectorıs in
90 per cent of subjects afflicted with the disease
The activity of the adrenal secretory mechanısm may
be reduced by ırradıatıon of the adrenal glands
Patients so treated, who show a reduction in the
severity or frequency of attacks, no longer respond to
the precıpıtatıng factors mentioned above by an
adrenal dıscharge Those who do not ımprove con-
tınue to show the response *Paul Wood*

**Disadvantages of Thiouracil Treatment of Angına
Pectoris** J R DiPALMER and J J MAGOVERN
Amer Heart J, 32, 494-503, Oct , 1946

Eight patients with angına pectoris who had been
under observation for several years were gıven
thıouracıl (usually 0 6 g daıly) for periods rangıng

from 3 weeks to 14 months The effects on their anginal pain, exercise tolerance, and basal metabolic rate were studied Difficulty was experienced in lowering the basal metabolic rate of the optimum level of -10 to -20 per cent, at which levels the anginal pain was less severe, below these levels the patients became too myxœdematous The authors believe that there is a tendency for water retention to occur as the metabolism is lowered, so that pulmonary œdema and increased dyspnœa appear Two patients developed toxic skin rashes Four of them benefited from the thiouracil, but in only 2 of these was the improvement marked Both of these had a raised basal metabolic rate before treatment, a finding which is considered the only indication for use of the drug other than as a therapeutic test in the selection for thyroidectomy of patients with angina pectoris

B McArdle

The Treatment of Angina Pectoris by Irradiation of the Adrenal Glands, Clinical Experience R L McMillan and J P Rousseau *N C med J*, 7, 550–553, Oct, 1946

The adrenal glands of 23 patients with severe angina pectoris were irradiated, each adrenal area receiving 600 r in three divided doses over a week Thirteen patients were greatly relieved, 4 moderately so, 3 slightly, and 3 not at all The period of observation was 2 to 12 months Two of the patients who most benefited died suddenly during this time, and a third died from probable myocardial infarction Blood pressure readings did not change significantly in the males, but showed an average drop of 23/22 mm in the females On the whole, patients seemed less emotional after treatment The most severe cases, and those in which attacks were especially provoked by emotion, did best The subsequent incidence of myocardial infarction and the life expectancy are assumed to remain unaltered *Paul Wood*

Cardiac Muscle Further Studies, Investigation of Chemical Changes in Myocardial Insufficiency with Special Reference to Adenosinetriphosphate G H Mangun and V C Myers *Arch intern Med*, 78, 441–446, Oct, 1946

The creatine, the total phosphorus and acid-soluble phosphorus, and possibly the potassium content of a failing heart muscle are usually decreased In the dog with myocardial insufficiency due to induced aortic incompetence, Mangun and Roberts had noted a marked decrease in the adenosine-triphosphate and phosphocreatine content of the left ventricle The present authors use a new method for the estimation of total acid-soluble purines and of oxypurines, which involves hydrolysis of purine compounds, deamination with nitrous acid, precipitation with copper

bisulphite, and estimation of the nitrogen content of the precipitate They claim that the acid-extractable purine content of the left ventricle, calculated as adenine, is decreased in myocardial insufficiency Lowered concentrations of purine were also observed in the myocardium of the right ventricle in some, but not in all, cases of pneumonia *Henry Cohen*

Disseminated Parenchymatous Ossification in the Lungs in Association with Mitral Stenosis A Elkeles and L E Glynn *J Path Bact*, 58, 517–522, Sept, 1946

The case described is of a man of 32 years who died of congestive heart failure due to mitral stenosis, before death X rays showed numerous dense miliary shadows on both sides, the typical cardiac outline of mitral stenosis was also present At necropsy the lungs showed brown induration and there were 2 small infarcts Microscopically the radio-opaque nodules were found to be true bone, filling groups of alveoli and extending into the alveolar ducts, there were also small amorphous calcareous fragments lying in alveoli and occasionally capping the bony structures Sections stained for elastic tissue showed the remains of the interalveolar structure contained within the bone The other lung lesion of interest was an active rheumatic inflammation of arteries intimal proliferation, medial fibrinoid necrosis, and adventitial histiocytic infiltration, there was also chronic passive congestion and interstitial fibrosis The heart showed a severe degree of mitral stenosis and there was also evidence of aortic incompetence

W S Killpack

Miliary Appearances and Manifestations of Pulmonary Stasis in Mitral Disease M Leblanc *Arch Mal Cœur*, 39, 69–74, March–April, 1946

The case is reported of a man who was known to have had rheumatic carditis since the age of 20 and some dyspnœa since the age of 41 There were signs of mitral stenosis, auricular fibrillation, and systemic congestion His blood pressure was 165/115 mm Chest skiagrams showed, in addition to the heart of mitral stenosis, a generalized marbling of the lung fields, most marked in the mid-zones This appeared to be due to two elements—small cavities and miliary nodules—which together suggested pulmonary tuberculosis The sputum was negative for tubercle bacilli Treatment for cardiac failure was given, and after 2 months symptoms were relieved, but the X-ray appearance of the lungs was unchanged apart from the absorption of a pleural effusion The miliary pulmonary nodules which are a rare feature of mitral stenosis are said to be composed of " heart-failure cells " and blood pigment derived from extravasated red cells *Harold Cookson*

ELECTROCARDIOGRAPHIC STUDY OF TYPHOID MYOCARDITIS

BY

F MAINZER

From the Department of Internal Medicine, The Jewish Hospital, Alexandria, Egypt

During the last century the conception of circulatory failure in the course of acute infectious diseases has been subjected to changes in several instances   Circulatory failure of every kind has, of course, a serious influence on the action of the heart itself, and for this reason in infectious diseases it was considered in those early days (1860–95) as heart failure, and the anatomical damage of the myocardium was much investigated, especially by French authors

A revolution of this conception was brought about by the investigations of Romberg and Paessler (1899), they showed the paralytic effect of bacterial toxins on the vasomotor centre and considered circulatory failure in infectious diseases merely as a paralysis of the peripheral blood vessels, the heart failure being mainly due to the condition of shock from the infection   This interpretation has been widely accepted till our days

Later it was shown that in a considerable number of infectious diseases electrocardiographic changes can be found   This fact could apparently be related to the previous findings of myocardial damage   Indeed anatomical damage to the heart muscle occurring in a number of infections, especially rheumatic fever, diphtheria, scarlet fever, variola, and more rarely in cerebrospinal fever and other diseases, as well as in typhoid fever which is discussed in this paper, has been described during the second half of the nineteenth century

Electrocardiographic changes were found in acute infections such as rheumatic fever, diphtheria, pneumonia, scarlet fever, streptococcal sore throat, cerebrospinal fever, typhus, Malta fever, grippal infections, cholera, and epidemic parotitis

Our own findings in a hundred typhoid cases will be described and discussed here

CARDIOGRAPHIC FINDINGS

In Egypt typhoid fever is a common disease, in our department there were between 80 and 120 admissions a year   The findings in 254 tracings from 106 cases are reported here, they are to be divided in 3 groups

Series I (1933–34) 39 cases   In these only one cardiogram was taken some days after the return of the body temperature to normal

Series II (1940–41) 60 cases   In these several cardiograms were taken (3–7) during the fever period and after the return to normal temperature, a total of 205 tracings

Series III (1933–34) 7 cases   These were cases treated with chinin-bismuth-iodide   For reasons to be discussed below they are put together in a separate series, there was only one tracing as in series I

The cardiograms were made with an amplifier electrocardiograph in the three limb leads and in lead IV F   During the period 1933–34 before the standardization of the præcordial leads we took lead IV F with inverted poles, in some cases of this period no præcordial lead was taken   Some technical difficulties arose from the need to take the tracings in

M

the wards and the unco-operative attitude of stuporous typhoid patients   and during the war
the recording paper was of a very unsatisfactory quality, resulting in poor tracings

Most of the patients suffered from *Eberthella* infection, and some from infection with
Salmonella paratyphi (Paratyphoid A) or *Salmonella Schottmuelleri* (Paratyphoid B)   The
diagnosis was clinically certain in all cases and was confirmed by laboratory findings in all but
two   Patients with a history or clinical signs of previous heart disease were not included in
this report   Table I shows the laboratory findings

TABLE I
LABORATORY FINDINGS IN TYPHOID CASES

Diagnostic procedure	Eberthella typhosa (T)	Salmonella paratyphi (A)	Salmonella Schott-muelleri (B)	Mixed infection T+B	Totals
Blood culture	6	—	—	—	6
Stool culture	49	1	4	2	56
Agglutination	27	2	13	—	42
Totals	82	3	17	2	104
Clinical diagnosis only					2
					106

If the blood-culture had a negative result, a frequent happening since the patients were
admitted to the hospital at too late a stage of the disease, a stool-culture was done and
repeated, if necessary, in cases with negative blood- and stool-cultures the agglutination test
was made to confirm the diagnosis, consequently all patients registered in Table I as positive
stool-culture had a negative blood-culture, and all registered as positive agglutination test
had negative blood- and stool-cultures

Of the 106 patients 7 died in the course of the infection   The causes of death were toxic
circulatory failure in 2 cases (1 with acute nephrosis), intestinal perforation in 2 cases, and
typhoid myocarditis in 3 cases

The clinical picture of heart failure in typhoid myocarditis is very different from heart
failure in valvular disease in its quick development, and resembles myocarditis in diphtheria
in the combination of " forward failure " and " backward failure ", so in serious cases the
extreme weakness and apathy, the moist and cold lividness of the skin with low blood pressure
and insufficient pulse pressure of the " forward failure " is combined with engorgement and
tenderness of the liver, congestion of the lungs, cyanosis, and sacral œdema, the heart sounds
are dull and often a systolic murmur is present at the apex, there is always tachycardia, often
embryocardia, and sometimes gallop rhythm at the apex

The less conspicuous the symptoms are in slight cases, the more they fuse with the
phenomena of the peripheral circulatory failure at the acme of the fever, and so the more
important becomes the cardiogram for the diagnosis

First we shall describe these findings and afterwards discuss their interpretation   Table II
summarizes the frequency of electrocardiographic alterations in our observations

Changes observed only in leads III and IV F were neglected owing to the dependence of
their shape on the position of the diaphragm, so every registered abnormality was present
at least in one of the leads I and II

Columns B and C of Table II include patients with tachycardia or bradycardia only
without other findings, since these changes occurred mostly combined with other cardiographic
abnormalities, it does not represent the total number with tachycardia or bradycardia

TABLE II

FREQUENCY OF ELECTROCARDIOGRAPHIC CHANGES IN TYPHOID FEVER

A Normal	B Tachy-cardia only (over 110)	C Brady-cardia only (under 60)	D A+B+C	E Slight abnormali-ties	F Moderate abnormali-ties	G Severe abnormali-ties	H E+F+G	Total
			Series I Electrocardiograms after disappearance of fever					
20	8	2	30	3	6	—	9	39
			Series II Electrocardiograms during and after the fever					
22	1	2	25	10	19	6	35	60
			Series III Electrocardiograms of patients treated with chinin-bismuth-iodide					
1	—	—	1	—	—	6	6	7
			Total					
43	9	4	56	13	25	12	60	106

" Slight " cardiographic alterations included moderate decrease of voltage of the ventricular and final complex, if present in several leads Of course the classification of " slight," " moderate," and " severe " is somewhat arbitrary, but does not prejudice the conclusions to be drawn

Table II shows cardiographic changes in a little less than two-thirds of the examined cases, if the tracings were taken during and after the fever period (series II), such changes were present in less than half, if tracings were taken only in the convalescent period, this result agrees with Table III showing that these changes persist only in half of the cases after the end of the fever period

Special discussion is needed for the 7 patients treated with chinin-bismuth-iodide (series III) Here intramuscular injections of chinin-bismuth-iodide in oily suspension were made twice a week, 2–3 ml according to the age (=0 05–0 075 g metallic bismuth), a total of 6–8 injections in every case These patients with one exception developed serious circulatory failure in the course of the typhoid infection, the only exception was a mild case that received only 3 injections All the 7 presented during convalescence severe cardiographic alterations indicating myocardial damage We abstain from deciding if there was a causal relation between this treatment and the constancy of heart muscle involvement

Changes of the final complex were the most frequent abnormality, T was flattened, absent, or negative in two or more leads (changes present alone in leads III and IV F were not considered) Often the S–T segment was below or above the zero-line The ventricular complex often showed low voltage with slurring or notching Right or left axis deviation was not infrequent in several instances we noted a high voltage Q in two leads (leads I and II or leads II and III) Mostly these cardiographic changes occurred together and combined with tachycardia or bradycardia, the latter in young patients with pronounced or sometimes extreme respiratory arrhythmia, there were curves resembling digitalis tracings by the combination of a slow pulse rate (with respiratory arrhythmia) with inverted T waves A prolonged P–R interval, described elsewhere as a frequent happening in typhoid fever (Porter and Bloom, 1935) was present in one instance only and was not permanent

In earlier papers the frequency of the different cardiographic alterations is mostly registered by tables Here in view of the great number we prefer to reproduce the curves of a few illustrative cases

Case I A man, aged 21, with an unimportant previous history was admitted after a six days' fever on 11/4/40 with a temperature of 40° C (rectal) The pulse rate was 96 a minute The heart was slightly enlarged to the left, with a systolic murmur at the apex The spleen was palpable Moderate anæmia existed hæmoglobin, 65 per cent (10 4 g), erythrocytes, 3,900,000, and leucocytes,

M*

7000 In the urine there were traces of albumin, tests for urobilin and urobilinogen were positive The blood-culture was positive for *Eberthella typhosa*, the agglutination test 1 150 The fever fell after one week to between 38° C and 39° C and after three weeks to below 38° C The heart enlarge-ment to the left increased The liver became congested and tender With temperatures about 37 5° C the circulatory failure increased, the pressure decreasing from 130/55 to 95/75 mm Neither strophanthine given intravenously nor vasomotor stimulants (caffeine, coramine) nor cortico-supra-renal hormone (percorten) could stop the failure Death occurred after a 57 days' illness with the signs and the symptoms mentioned above

A
B
C
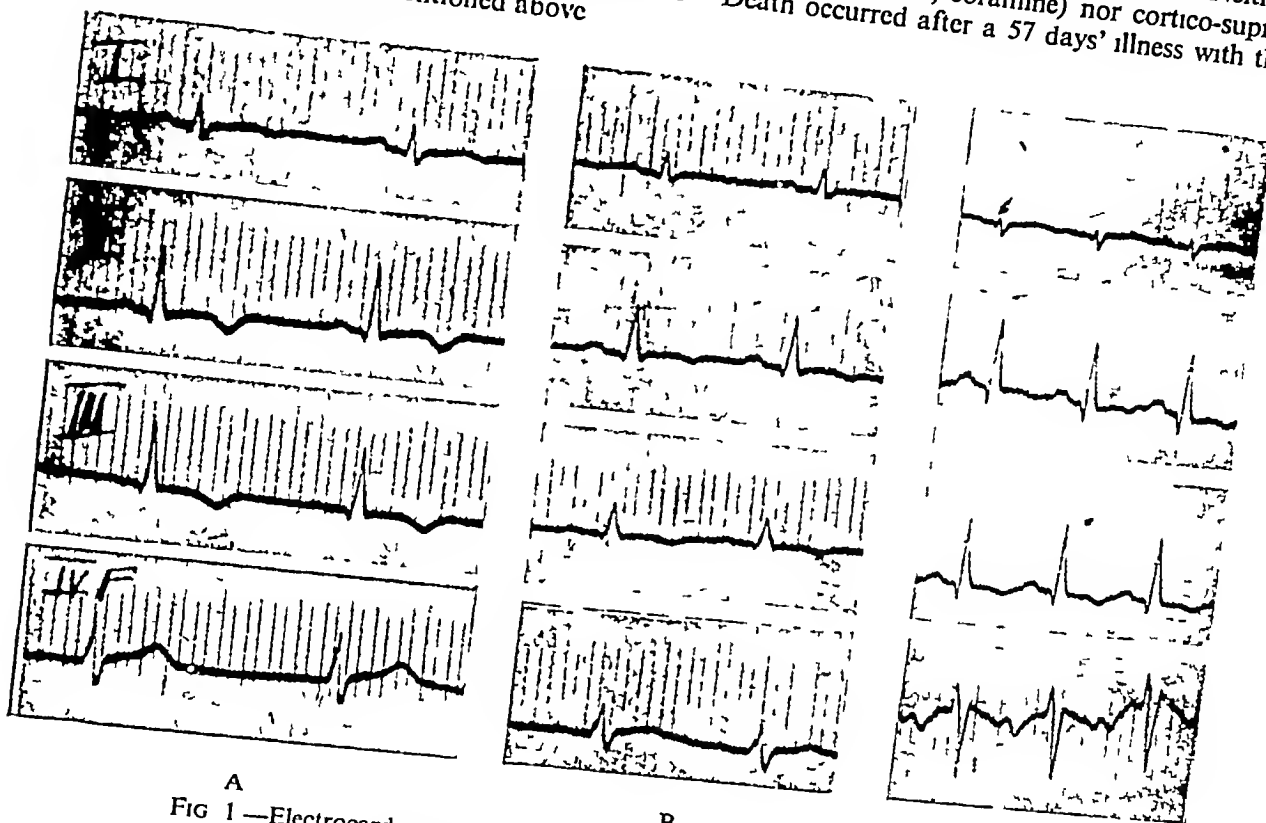
FIG 1 —Electrocardiograms of a case of typhoid myocarditis with fatal issue

	Date	Body temperature	Pulse rate	P-R	R-S (in seconds)	R-T
(A)	19/4/40	38 7° C	76	0 12	0 08	0 35
(B)	5/5/40	38 5° C	107	0 16	0 07	0 33
(C)	30/5/40	37 6° C	156	0 13	0 07	0 23

In Fig 1A, T is negative in the three limb leads, and deeply in leads II and III In Fig 1B, 24 days later, with the increasing pulse rate the voltage of the ventricular complex and of the final wave has diminished, so the T waves are now nearly flat Fig 1C, two days before death, shows also a further increase in the pulse rate and the appearance of a Q wave in leads II and III and diminished voltage of R-T Changes of the lead IV E are not considered in view of the difficulty of replacing the chest-electrode always at the same spot and the influence of the variable position of the diaphragm

Case 2 A seaman, aged 31, with an unimportant previous history was admitted to the hospital after a six days' fever on 25/7/40 with the typical picture of typhoid fever There was a rose rash on the skin of the abdomen The spleen was enlarged Blood hæmoglobin, 102 per cent (=16 4 g), erythrocytes, 5,200,000, leucocytes, 5700 The blood-culture was positive for *Eberthella typhosa* After one week with a temperature between 39° C and 40° C it became subfebrile within the range of 37 5° C by lysis Convalescence was uneventful and the patient was discharged on 8/11/40 In the beginning of the disease the heart sounds were very dull, other peculiarities of the circulatory system were not present Of the series of six curves we have chosen four for reproduction, only the first tracing had been taken during the fever period, the other three during convalescence

A   B   C   D
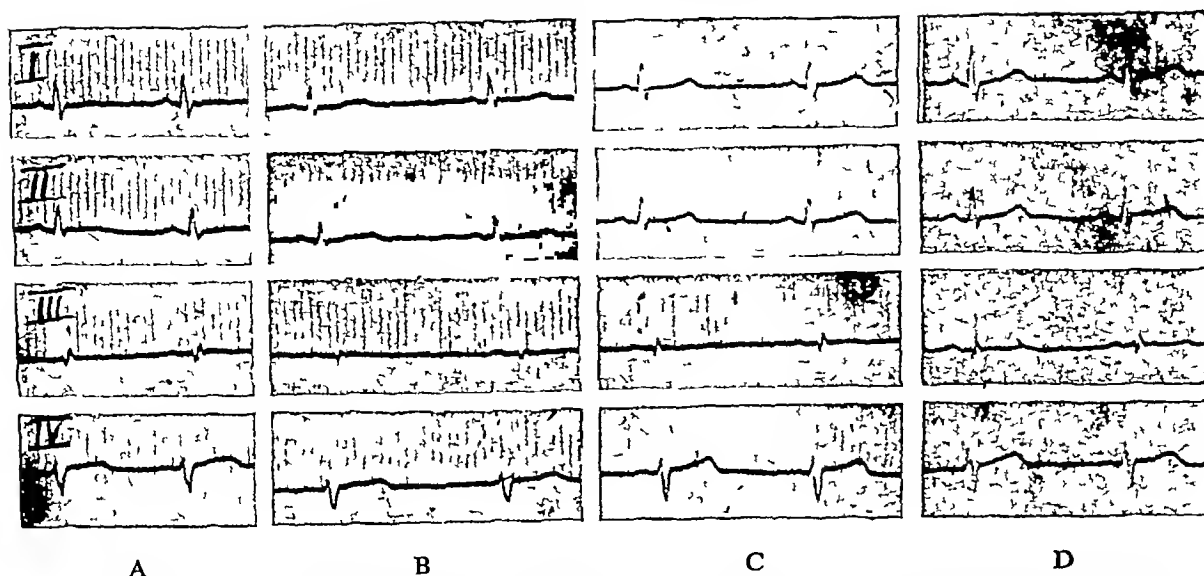
Fig 2 —Electrocardiograms of a case of clinically latent typhoid myocarditis with cure   (Reduced to three-fifths)

	Date	Body temperature	Pulse rate	P–R	R–S	R–T
					(in seconds)	
(A)	3/8/40	38 5° C	75	0 13	0 08	0 35
(B)	12/8/40	37 1° C	65	0 12	0 08	0 38
(C)	21/8/40	36 9° C	63	0 15	0 07	0 38
(D)	31/8/40	36 9° C	70	0 17	0 08	0 37

In Fig 2A, there is a notable flattening of the T wave, which in all leads is only just present, there is also a moderate decrease of voltage of the ventricular complex compared with later tracings   The changes disappeared slowly and step by step   The bradycardia, very pronounced in the beginning. disappeared likewise gradually

Case 3   A girl, aged 18, with unimportant previous history was admitted to the hospital after a five days' fever (on 15/11/33) with the clinical picture of an exceptionally serious typhoid fever

The blood-culture was positive for *Eberthella typhosa*   Blood haemoglobin, 52 per cent (8 3 g), erythrocytes, 3,000,000, leucocytes, 6000   The course of the disease was likewise very serious   The fever between 39° C and 40° C lasted during two months including two relapses of short duration After a week's stay at hospital a slight intestinal haemorrhage occurred   Without peculiarities of the heart itself the circulation was in a critical condition from the beginning for six weeks   At the time of discharge, tachycardia persisted with a pulse rate about 150 after slight exertion   There were three electrocardiograms without praecordial leads (1933)

In Fig 3A, the T waves are negative in all three limb leads, the S–T segment is below the zero-line in leads I and II   The A-V conduction time is conspicuously prolonged with P–R of 0 23 sec   After a fortnight convalescence with normal temperatures (Fig 3B) the cardiographic changes had disappeared only partially, the final complex in lead II being abnormal, after a further month (Fig 3C) the tracing was normal in spite of the clinical instability of the circulation

Case 4   A girl, aged 12, was admitted to the hospital on 4/12/34 with a fever of three weeks' duration   For one week the fever had ranged between 39°–40° C , but previously there had been subfebrile temperatures   Before the admission to the hospital a blood-culture was positive for *Salmonella Schottmuelleri* (*Paratyphosus B*)   The course of the disease was uneventful with a month of fever between 39° and 40° C   During the fever period relative bradycardia existed with pulse rates about 100, in convalescence it rose to 120 and after slight exertion to 140–160 and remained so during three months   During the first 3 weeks after admission the patient received twice a week intramuscular injections of chinin-bismuth-iodide in oily suspension (0 05 g bismuth per injection) The tracing taken on the fifth day without fever shows notable changes of the final complex   T is negative in the limb leads and the S–T segment in leads II and III is below the zero-line and fused with the initial branch of T

A   B   C
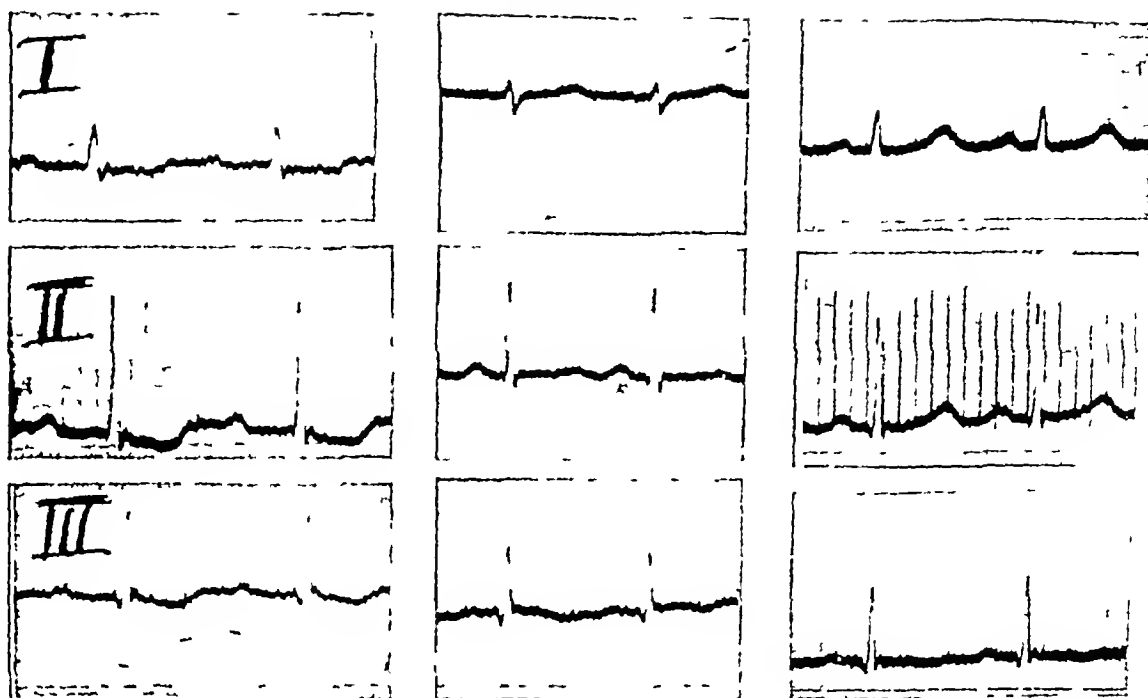
FIG 3 —Electrocardiograms of a cured case of typhoid myocarditis with temporarily prolonged A-V conduction

	Date	Body temperature	Pulse rate	P-R	R-S (in seconds)	R-T
(A)	9/10/33	38 7° C	110	0 23	0 07	0 35
(B)	8/11/33	37 1° C	144	0 13	0 06	0 36
(C)	18/12/33	37 0° C	134	0 05	0 05	0 28
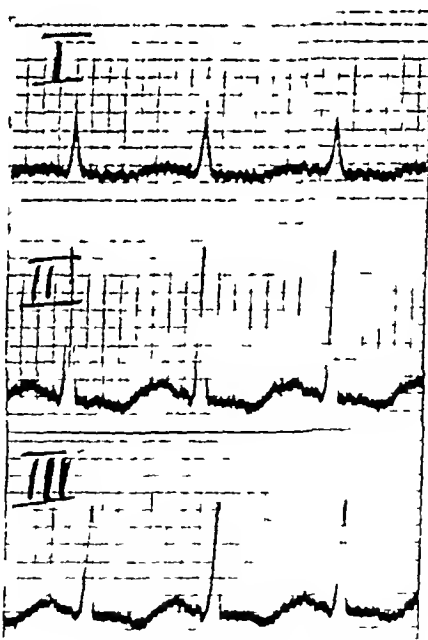
FIG 4 —Electrocardiogram of a case of typhoid myocarditis in a patient treated with chinin-bismuth-iodide (taken after convalescence)

Date	Body temperature	Pulse rate	P-R	R-S (in seconds)	R-T
9/1/35	36 8° C	132	0 15	0 06	0 25

The time relation between the cardiographic changes and the infectious fever is not only interesting from the pathological point of view, but is also important for the interpretation of the tracings   The question is, if there is any parallelism between the fever as a measure of the infectious process and the development of cardiographic abnormalities   For this purpose we must examine (1) which is the phase of the infection giving rise to the cardio-graphic alterations, and (2) whether the changes disappear during the fever or persist after the fever with normal temperatures   Series II of Table II is a satisfactory basis for this examination   Out of the 35 patients in column H, 12 are not considered because of the insufficient number of tracings, this includes 5 fatal cases, 3 of them dying from typhoid myocarditis   In the remaining 23, the abnormal tracings persisted in 18 cases during convalescence, their disappearance lasted mostly from one to three weeks, in some instances even more   Abnormalities persisting indefinitely were not observed   But tachycardia between 120 and 140, especially after slight exertion, was often present many weeks after the recording of otherwise normal tracings   In three cases the changes disappeared during the fever period   In one case there was a complete correlation between the fever and the intensity of the cardiographic changes   In another case they developed only after that the infection lasted, with normal temperatures

COMMENT

Electrocardiographic abnormalities in typhoid fever, although in a restricted number of observations, were described by several investigators (Bowe, 1929, Chagras, 1931, Master Romanoff, and Jaffe, 1931, Lessard, 1933, Porter and Bloom, 1935, and Kiss and Wolleck, 1935)   It is known that fever by itself, physically induced, can produce electrocardiographic changes (Vesell and Bierman, 1936, Knies, 1941, Clagett, 1944)   these abnormalities, however, are slight

In typhoid fever anatomical damage of the myocardium is regularly present   as early as in the second half of the last century this fact has been observed by several investigators (Hayem, 1869, Landouzy and Siredey, 1887, Romberg, 1893), cloudy swelling or hyaline degeneration of the myocardial fibres with necrotic foci of microscopic size and infiltration of the heart muscle, interstitial or focal, may be found

In typhoid fever a shock-like peripheral circulatory collapse exists, in shock, as is well known, cardiographic changes similar to those in coronary insufficiency can occur (Scherf and Klotz, 1944)   In our observations, however, the changes persisted longer than the fever and disappeared only slowly during convalescence, in one case they developed even after recovery from the fever   In view of these time relations a causal connection between the peripheral circulatory disturbances and the cardiographic changes cannot be assumed (even if at the acme of the infection the peripheral failure can contribute temporarily to their development)

Vagal stimulation might be a factor in producing changes of the final complex with reference to their combined occurrence with bradycardia (and respiratory arrhythmia), however, the same alterations were found, and even more frequently, associated with tachycardia

Severe anæmia can also alter the cardiogram (Bauge, 1933, Bloch, 1937, and Szekely, 1940), in our cases severe anæmia was only exceptionally present, and jaundice (Meier, 1940) was seen in only one instance

In typhoid fever as well as in other infections, anatomical damage of the suprarenal glands is a common finding (Dietrich, 1918, and Dietrich and Siegmund, 1936), and cortical failure has been supposed to be a factor in the development of the circulatory shock   the curves of the Addisonian crisis, however, are very different from those in typhoid fever or in other infections (Delius and Opitz, 1935, and Goodof and Macbryde, 1944), they are characterized by tall, narrow, upright T waves

Finally B-avitaminosis could be suspected as a factor intervening in the development of typhoid cardiograms, produced by lack of thiamin (Weiss and Wilkins, 1937, Dustin, Weyler, and Roberts, 1939, and Schott, 1944), or of niacin (Feil, 1936, and Mainzer and Krause, 1940) For a long period medical science recommended diets for typhoid fever that were essentially hunger diets, furthermore, it is often difficult to feed these patients sufficiently In our department a high-calorie diet with vitamin preparations was customary, vitamin deficiency could have occurred only exceptionally

So the cardiographic alterations in typhoid fever can be referred to the anatomical damage of the myocardium produced by the infection, the tracing is the expression of the typhoid myocarditis

The myocarditis is the cause of death more often than the diagnosis is made It is easily overshadowed at the acme of the infection by the peripheral circulatory disturbance, the clinical manifestations of this myocarditis, tachycardia and circulatory instability after exercise, only become manifest in convalescence and persist for a longer time in most cases than the cardiographic alterations

SUMMARY

The electrocardiographic findings of 106 cases of typhoid fever are described In 35 of 60 patients cardiographic abnormalities (other than tachycardia or bradycardia with or without respiratory arrhythmia) were encountered during the infection, in 18 they persisted during convalescence, in 1 they developed only in this period In 12 cases the time relation between the infection and the development of the cardiographic changes could not be observed for technical reasons (lack of a sufficient number of tracings, death during the infection, etc)

The cardiographic abnormalities take mostly between one and three weeks to disappear (after the onset of the convalescence) Clinical phenomena indicating an instability of the circulatory system (tachycardia) frequently persist for a long time (1 to 3 months) after the disappearance of the cardiographic changes

Out of a series of 106 patients the cardiograms taken during convalescence were abnormal in 60 instances Deformations of the final complex were most frequently observed flat or negative T waves and displacement of the S–T segment Appearance of abnormal Q waves, development of left or right axis deviation, decrease in voltage, slurring or notching of the ventricular complex were also common findings In one case a temporarily prolonged A-V conduction was present

By excluding the possible influences of other factors on the cardiogram (fever, peripheral circulatory failure, suprarenal insufficiency, jaundice, B-avitaminosis) it is shown that the abnormal tracings can be referred to the anatomical damage of the myocardium

The clinical picture of typhoid myocarditis is described with reference to three fatal cases The disease is often overshadowed at the acme of the infection by signs of peripheral circulatory failure, escaping diagnosis during the fever period and becoming clinically manifest only during convalescence The cardiographic diagnosis was made always during the fever period with one exception The clinical phenomena of the myocardial damage often persist longer than the cardiographic abnormalities

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HEART-VECTOR AND LEADS PART II

BY

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In a preceding paper (Burger and van Milaan, 1946) we have treated the problem of the relation between the heart-vector and the leads that are usual in electrocardiography Therein we pointed out that this relation is given by three linear equations, characterized by nine coefficients The value of these coefficients was determined by means of a model of the human body, a glass phantom filled with an electrolytically conducting liquid An artificial heart was used to put up an electric current field in the liquid, and the potential differences caused by this field were measured at the extremities L, R, and F

The human body, however, is not a homogeneous conductor and especially, the lungs, the spinal column, and the liver cause a lack of homogeneity Further, not only the leads from the extremities are of interest, but the increasing importance of the præcordial leads made it necessary to extend the method to other electrodes as well as to the extremities The component of the heart vector, directed horizontally from the back to the chest (Y-component) is in this case of preponderating importance We shall describe an improvement of our former method, allowing for the points mentioned above

THE NEW PHANTOM

To be able to install the internal organs and to fix the electrodes at different points on the surface of the body, the phantom had to be constructed in such a way that its inner side was within reach It was of michaplast, that had formed the cover of a small statue of a human being on a scale of 1 3 So it had the normal proportions of a true human body It was cut into two pieces by a plane parallel to the frontal plane of the body Of the two pieces the chest-side was the larger one and formed a small basin (Fig 1) standing on the table, the phantom lying face downward Arms and legs of the phantom were only short stubs, as the current does not penetrate in them This part was placed in a large basin, filled with a solution of copper sulphate The back-side formed a cover, in which holes were drilled to let the air escape A broad flange prevented the current-field from leaking to the outside

The artificial heart H consisted of two parallel copper plates of 1 0 cm diameter and 1 0 cm apart The space between was filled with an insulating substance (Burger and van Milaan, 1946, p 159) It was fixed to a glass tube T, that protruded from the back-cover of the phantom One heart, with its axis perpendicular to the glass tube, was turnable on a vertical axis, a dial D indicating its direction Herewith it was possible to set up the component of the heart-vector, perpendicular to the median plane of the body (X-component), or of the component in the direction of its length-axis (Z-component) Another heart gave the component, vertical in the phantom (Y-component) Either heart was placed in the normal position A potential difference of 4 volts set up the current field inside the phantom

In addition to the extremity electrodes, L, R, and F, we have used a series of electrodes in different places Pieces of copper foil of 1–0 5 sq cm , connected to an insulated wire, were fixed to the inner wall of the phantom in the desired position The potential difference
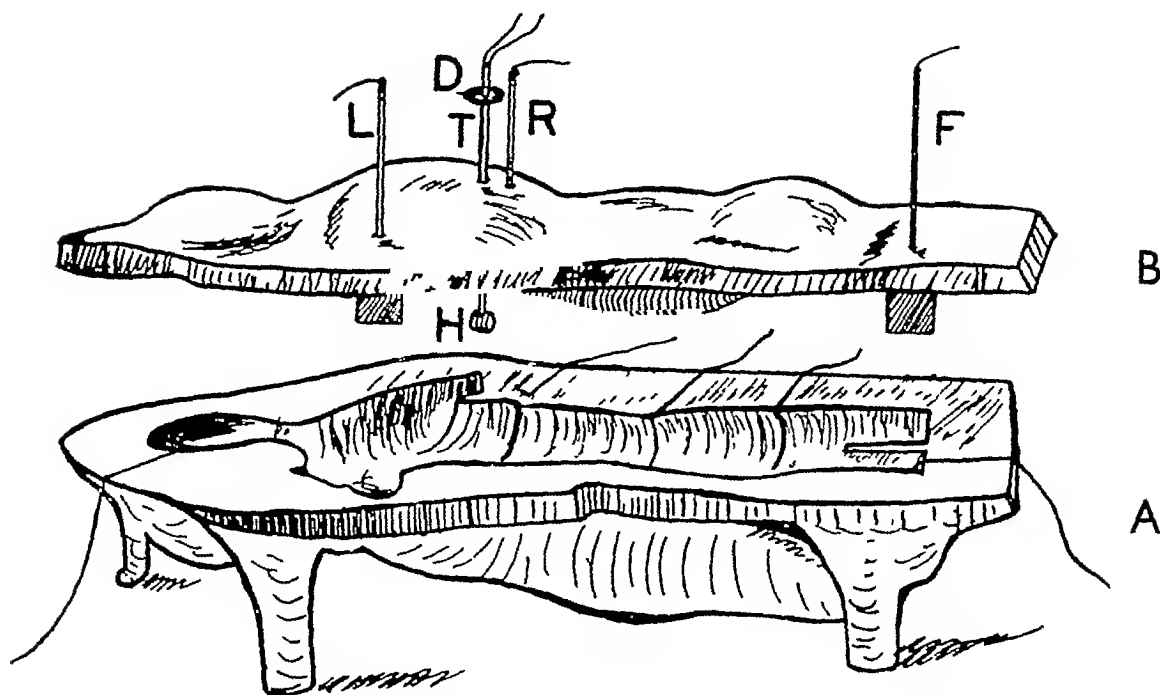
FIG 1—Phantom to measure the coefficients in the relation between heart-vector and leads
    (A) chest-side   (B) back-side
    L, R, and F   extremity electrodes
    H   artificial heart with protruding glass tube (T) with dial (D)

between two electrodes was measured by means of a galvanometer provided with a high resistance

We have asked if the back-cover was essentially necessary   Indeed it proved to be that the potential differences were of an entirely different value if the back-cover was omitted, the heart being placed in the same position   Even if the back-cover was elevated only a few millimetres, the change was perceptible   So we must conclude that measurements with an open basin cannot have any quantitative significance (Guckes, 1939, Hess, 1935, Hollman and Hollmann, 1937, Molz, 1939, and Schellong, 1939)

The lungs in the human body must have a great influence on the current-field of the heart, as their specific resistance is so much greater than that of the other parts of the body   this is a consequence of the air they contain   From anatomical data of the volume of the lungs and physiological data of their air content we have roughly calculated their specific resistance, and that in the state of maximal inspiration, maximal expiration, and in the normal condition The specific resistance of the lung tissues was supposed to be the same as the average of the rest of the trunk   The result was that the lungs conduct about four times less than that rest

This ratio can be verified as follows   Formerly we have measured the mean specific resistance of the trunk in the above-mentioned three states of the lungs (Burger and van Milaan, 1943)   These specific resistances can be calculated approximately from anatomical date of the trunk, accepting the value of the specific resistance of the lungs, mentioned above

The substance of which the artificial lungs have to be made must have a specific resistance, four times greater than that of the surroundings   We have found that sand in an electro-lytical solution fulfils this requirement   We have, therefore, made two bags of cotton, the shape of which was, as accurately as possible, that of (real) human lungs   They were filled with sand and at their inner sides we have modelled to the best of our ability the hollows for the heart with needle and thread   It was, however, not possible to give them at the foot side the excavation of the pleural dome   The lungs were placed in the chest-part of the phantom

Some nipples, fixed to its wall, kept the lungs at some distance from it   In this way a conducting layer was left free, just as is the case between the human lungs and the chest wall

The artificial liver was made in the same way as the lungs   The liver, however, seems to have a specific resistance, depending greatly on circumstances, namely on the fat and blood contents   Our measurements show that the influence of the liver on the relation between heart-vector and leads is only small

Much greater is the influence of the spine, as it consists of badly conducting bone   The artificial spine was made of cork and was fixed to the back-cover   We have not tried to give it exactly the right shape, but we have given it the average cross-section of the true spine (on a scale 1 3)

RESULTS

The results of our measurements are all given in absolute units just as in our preceding paper   They hold good for a human body of average dimensions   The potential difference (lead) is expressed in volts, the heart-vector in volts $\times$ cm^2 The coefficients, therefore, in the equation

$$\text{Lead} = aX + bY + cZ \quad (X, Y, \text{ and } Z = \text{components of the heart vector}) \qquad (1)$$

are expressed in volt/volt cm^2 = cm^{-2} They are inversely proportional to the dimensions of the body
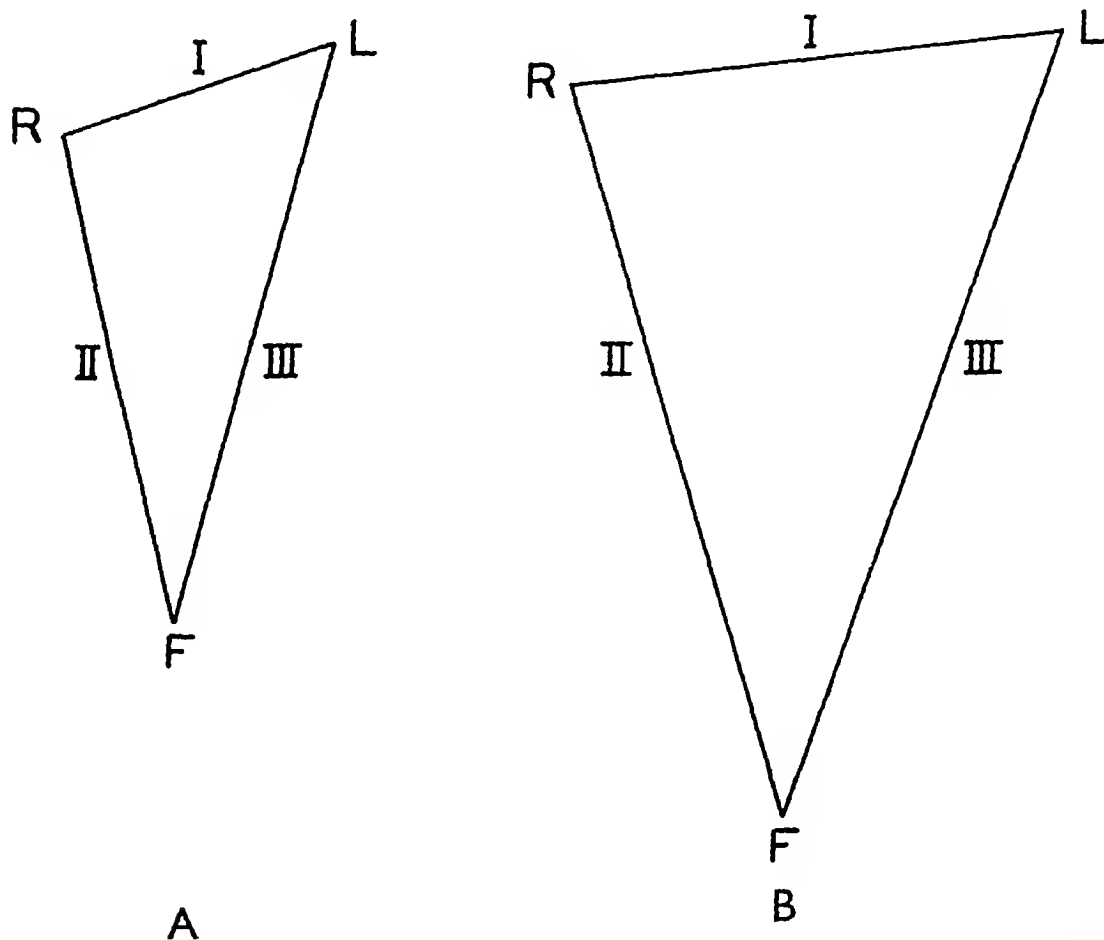
FIG 2 —(A) Triangle, representing the relation of heart-vector and leads, deduced from a phantom with lungs and spine   (B) The same, without lungs and spine

The measurement is performed in using an artificial heart giving the components X, Y, and Z one by one   Each time a lead is measured, and from the value of lead and component the corresponding coefficient is to deduce as quotient of lead and component

Limb Leads

First we have checked our method by measurements of the limb leads of the phantom without internal organs   The result was in accordance with our preceding measurements with the glass phantom

The influence of the lungs was very marked   The contribution of the horizontal component (X) to lead I especially was reduced appreciably by the lungs   This was to be expected, as the badly conducting lungs at both sides of the heart screen off the current in a direction from the right arm to the left one   The spine did not alter the ratio of the leads appreciably but their absolute values were increased   The liver altered the leads so slightly, that, as a rule, we have omitted it

The numerical result with the phantom, provided with lungs and spine, is given in the following formulæ

$$\left.\begin{array}{l} \text{I} = (65X - 21Z) \times 10^{-5} \\ \text{II*} = (-25X - 120Z) \times 10^{-5} \\ \text{III} = (-40X + 141Z) \times 10^{-5} \end{array}\right\} \qquad (2)$$

The mathematical consequence of this analytical relation between heart-vector and leads is that it may be represented geometrically   In Fig 2A we give this representation, coming in place of the well-known triangle of Einthoven   Fig 2B represents the relation between leads and heart-vector as found with the phantom without internal organs   The leads I, II, and III are proportional to the product of the projection of the heart-vector on the sides of this triangle and the length of the side on which it is projected

Præcordial Leads

Up to now we have treated the problem as a two-dimensional one   Only the components X and Z parallel to the frontal plane, were taken into account   But as a matter of fact the problem is a three-dimensional one (Schellong, 1939), the heart-vector has also a Y-component, horizontal and parallel to the medium-plane   We will call it positive if it is directed from back to chest   Fig 3 gives the situation of the three components of the heart-vector

To find all the three components X, Y, and Z of the heart-vector we need three equations, so we have to measure three independent leads   The extremity leads I, II, and III cannot serve this purpose, as they are dependent, their sum being zero   To get the three independent equations necessary to determine unambiguously the three components of the heart-vector, at least one more electrode has to be used   As such an electrode one of the usual præcordial leads (IV) is suitable   As the position of lead IV we have taken a point in the mammary line and in the fifth intercostal space   We have measured the potential difference between IV and the left foot (F)   It appeared to be

$$\text{IV} = (19X + 30Y + 20Z) \times 10^{-5} \qquad (3)$$

FIG 3 —Heart-vector $\overline{H}$ and its rectangular components X, Y, and Z

This equation must be combined with two equations for the leads I and II, in which the component Y is

* For reasons of symmetry lead II is given the opposite sign to the usual

not omitted   These equations are obtained by putting in the equation (2) the term with Y, provided with its coefficient, found with the phantom   These equations are

$$I = (65X - 17Y - 21X) \times 10^{-5}$$
$$II = (-25X - 15Y - 120Z) \times 10^{-6}$$

(2A)

From the three equations (3) and (2A), it is possible to solve X, Y, and Z   The result is

$$X = (12\,9\,I - 1\,2\,II + 6\,4\,IV) \times 10^{2}$$
$$Y = (-7\,0\,I + 6\,4\,II + 32\,8\,IV) \times 10^{2}$$
$$Z = (-1\,8\,I - 9\,0\,II - 5\,6\,IV) \times 10^{2}$$

(4)

Using these coefficients, one can calculate the components X, Y, and Z of the heart-vector from the simultaneously measured leads I, II, and IV

The equations (2), in which the Y-component is omitted, give an erroneous result for the X- and Z-components, that we will call X' and Z'   If X and Z are the true values of these components, we can prove that

$$X' = X - 0\,21Y$$
$$Z' = Z + 0\,17Y$$

(5)

We see, therefore, that the omission of Y gives a rather satisfactory value of the projection of the heart-vector, if its Y-component is smaller than X and Z

Neglecting the Y-component, from the equations (2) we can deduce an approximate value of the absolute magnitude of the heart-vector during its maximum (R)   Assuming for I a value of 1 mV and for II a value of −1 5 mV*) we find that the maximal R-deflection corresponds to a heart-vector of about 2 volt cm²

Just as in the two-dimensional case, it is possible in the three-dimensional one to give a geometrical representation Instead of a triangle we have to work with a tetrahedron, the angular points of which correspond to right arm (R), left arm (L), left foot (F), and præcordial electrode (IV) (Fig 4)   Each lead is the product of the projection of the heart-vector on the corresponding edge multiplied by the length of that edge   So if p is the projection of the heart-vector $\overline{H}$ on the edge RL, lead I is equal to p×RL etc The shape of the tetrahedron can be deduced easily from the coefficients of the equations (3) and (2A), giving the leads as a function of the components X, Y, and Z of the heart-vector

To solve the problem of the relation between heart-vector and leads completely, it would be necessary to measure the potential-difference between all the points on the surface of the phantom and a fixed point e g the left foot (F), and for the three components of the heart-vector   We do not know if there are leads that are to be preferred essentially above I II, and IV, nor do we know if there are arguments from the clinical side for using other ones

Fig 4 —Tetrahedron, representing the relation of heart-vector and leads

We have made some measurements with præcordial electrodes in the median-plane   The origin of the potential-differences was the Z-component of the heart-vector having unit value Fig 5 gives the potential difference between these electrodes and F, as a function of their distance

* As II has the opposite sign to usual, it has to be taken as negative
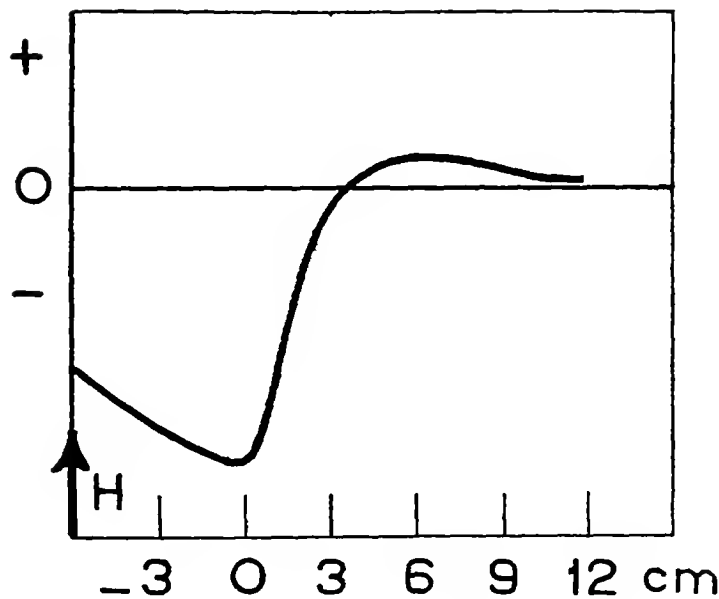
FIG 5 —Potential difference between præcordial electrodes in the median plane and the left foot (F) The numbers give the distance below the axillary line in the phantom H=head

below the axillary line   The point, denoted by H, represents the head, inside which the potential-differences can be neglected   The general type of the curve can be explained theoretically

Leads that depend on only one Component of the Heart-Vector

In equation (1) the coefficients a, b, and c depend on the position of the two electrodes It is possible to choose these in such a way that b and c both are zero   Then the lead is only depending on X, it is proportional to X Lead=aX   In the same way it can be arranged that the leads are depending only on Y and only on Z   Only with a phantom is it possible to find positions of the electrodes that fulfil these requirements

X-lead   The electrodes are placed respectively in the side, 12 cm below the axilla and on the right arm   X-lead=$1\ 56\times10^{-3}$X

Y-lead   The one electrode is placed on the chest wall, 9 cm to the left of the median plane and 27 cm below the axilla, the other is placed on the back in the median plane, 27 cm below the axilla   Y-lead=$2\ 4\times10^{-3}$Y

Z-lead   The electrodes are placed respectively on the left leg or foot (F) and on the throat 6 cm to the right of the median plane, at the height of the point of the larynx Z-lead=$1\ 0^{9}\times10^{-3}$Z

Only by experience can it be decided if these leads have any practical value

Short-circuiting of the Electromotive Action of the Heart by the Blood

The value of the heart-vector, deduced by the above method is only an effective one   The electromotive field strength of the heart muscle causes a current not only in the tissue surrounding it but also in the blood inside   As the latter is the better conducting material it acts as a shunt, the outer current being diminished by it (Beleradek and Noyons, 1923)   The value, therefore, that is found for the heart-vector is too small   From our measurements with the phantom it is impossible to find the true heart-vector   The construction of the artificial heart leaves this complication out of account

SUMMARY

The phantom used for the determination of the relation between heart-vector and leads has been improved   It has been provided with lungs and a spine and it is possible to apply electrodes in any desired position   The influence of lungs and spine is appreciable

The results of the measurements with lead IV and other præcordial leads are given

It is possible to find leads that depend on only one component of the heart-vector

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IDIOPATHIC CARDIAC HYPERTROPHY

BY

D G VULLIAMY

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At the beginning of the century idiopathic hypertrophy of the adult heart was commonly accepted as a diagnosis   since then a wider knowledge of the pathology has almost eliminated the term   Similarly in infants and children the disease entity known as congenital idiopathic cardiac hypertrophy is becoming rarer as more underlying causes are brought to light

The case here described is considered worth reporting because it appears to be an example of one type of infantile cardiac enlargement in which there are no signs of congenital heart disease at birth, but a rapid onset of symptoms and signs of cardiac failure in a previously healthy child, with a gross endocardial and myocardial fibrosis as the striking finding post-mortem

Case History

V H was admitted to Guy's Hospital under the care of Dr R W B Ellis, at the age of two years nine months   He was an only child of healthy parents and there was no family history of tuberculosis or other important illness

At birth he was a normal full term baby weighing 9¾ lb and there was no cyanosis following delivery   Breast feeding lasted for two months and was replaced by adequate artificial feeding including added vitamin extracts   His early development was normal, and he was walking at fifteen months of age   At one year he had pneumonia following measles, since when he had suffered from recurrent bronchitic attacks

A month before admission he had been an active, healthy child, but for three weeks he had shown signs of fatigue, listlessness, and irritability   Food was often refused and a hard dry cough became noticeable   There was no apparent loss of weight

On admission he was severely distressed, his face was flushed but the lips were not at that time cyanosed   There was dyspnœa, venous congestion in the neck, and pitting œdema of both ankles

The apex beat was diffuse and pulsation could be easily felt from the third to the sixth left intercostal spaces and from the mid-clavicular line out to the anterior axillary line   There was no increased cardiac dullness on percussion to the right of the sternum   A blowing systolic murmur was heard at the apex, and the blood pressure was 105/70 in both arms

A few scattered moist râles and rhonchi were the only abnormal physical signs in the lungs   The liver was enlarged and tender, reaching almost to the level of the umbilicus, but the spleen and kidneys were not palpable   Two days after admission the œdema had increased and there was evidence of a little ascites   Cyanosis was constant and dyspnœa was increased   Venesection of 45 c c of blood resulted in an improvement of the general condition

X-ray screening of the chest showed a heart greatly enlarged to the left and very slightly to the right   A film taken a few days later is reproduced in Fig 1 (see p 165)

A blood picture showed a slight hypochromic microcytic anæmia and a normal white

count   A glucose tolerance test, done with the object of excluding glycogen disease, was normal and showed no abnormal rise on administration of adrenalin

The urine showed no abnormal constituents   Ten days after admission an electrocardiogram showed right axis deviation with a wide notched QRS complex (Fig 2, see p 165)   A Mantoux test was positive to 1 10,000

The subsequent course of the illness, which lasted for nearly five months, was one of partial recoveries and relapses with a general trend towards increasing cardiac failure   During the periods of relapse, in which the patient became almost moribund, there was pyrexia between 100^c and $104°$ F , sometimes swinging in character, associated with signs of localized patchy consolidation in the lungs, particularly on the left side   White cell counts on these occasions showed a polymorph leucocytosis and blood culture was sterile   There was an apparent response to sulphadiazine, and the attacks were considered to be due to localized areas of lung collapse with superimposed infection   Therapy during the illness included digitalis, to which there was little response after the first relapse, and a course of vitamin B_1 as a therapeutic test for beri-beri, which also had no effect   An oxygen tent gave considerable relief during the relapses

A teleradiogram of the chest taken seven weeks after admission is reproduced in Fig 3 (see p 166), and shows an increase in the root shadows and some blurring of the heart outline

In view of the size and shape of the heart shadows and the positive Mantoux test, suggesting a possible diagnosis of tuberculous pericarditis, a diagnostic paracentesis of the pericardium was attempted during the third month   No pericardial fluid was, however, found

An alternative diagnosis of primary mediastinal neoplasm was suggested but screening failed to give any definite confirmation

During the following month the degree of cardiac failure gradually increased and finally a condition of generalized œdema followed by bronchopneumonia supervened and the patient died twenty-one weeks after admission

Autopsy   (Dr K J Randall, Pathology Department, Guy's Hospital)

There were numerous sub-pericardial hæmorrhages beneath both visceral and parietal surfaces   The pericardial sac contained about 100 ml of blood-stained fluid   The heart showed gross generalized enlargement, weighing 290 g and being of adult dimensions (normal heart weight for a child of 3 years=60 g)   The greatest thickness of the left ventricular wall was 1 8 cm , the maximum normal for an adult heart being approximately 1 0 cm   Apart from this gross hypertrophy there was considerable dilatation of all the chambers so that the thickness of the contracted heart wall would have been even greater

The myocardium was of normal colour and firm consistency   The endocardium, particularly of the left ventricle showed marked thickening of the " sugar icing " type   No congenital abnormalities of the heart or great vessels were present   The valves and coronary arteries were normal

Pleural effusions were present on both sides and the lungs showed early suppurative pneumonia   The mediastinal lymph nodes were moderately enlarged, but there was no sign of any tuberculous focus

The liver showed gross fatty change and chronic venous congestion   There were 500–600 ml of straw-coloured fluid in the peritoneal cavity

No other abnormality of any organ was found

On microscopical examination, the wall of the left ventricle showed a gross diffuse thickening of the endocardium by fibrous tissue   There was penetration of the fibrous tissue into the myocardium   This fibrosis was confirmed by staining with van Gieson's stain (Fig 4, see p 166)   No excess of glycogen was seen in sections stained by Best's carmine   There was no excessive lymphocytic infiltration of the muscle and no evidence of hyperplasia of the muscle fibres

Apart from the terminal suppurative pneumonia in lung sections and confirmation of the fatty change and passive venous congestion in the liver, no significant abnormality was seen in any other section

DISCUSSION

Kugel and Stoloff (1933) in a review of cases of so-called idiopathic cardiac hypertrophy of infancy and childhood published up to 1933, found from re-examination of the autopsy reports that out of a total of 52 cases, 17 could be regarded as pure idiopathic hypertrophy Of the remainder, 8 had inadequate autopsy reports and 27 showed various cardiac abnormalities, amongst which endocardial thickening and increased fibrous tissue in the myocardium were common findings   Round cell infiltration of the heart muscle was mentioned as occurring in 4 cases

In addition they reported in detail 7 new cases which they claimed might have been recorded as idiopathic hypertrophy had not careful histological examination of the heart been carried out   They all showed a similar picture, including thickening of the endocardium and patchy degeneration of muscle fibres with replacement fibrosis   Two of them showed excessive round cell infiltration, and in no case was there any abnormality of the values or the origin of the coronary arteries   An eighth case was added to the series by one of the authors (Kugel, 1939) in which a similar pathology was found and glycogen disease was excluded by special staining

In these eight cases, the ages ranged from three months to six and a half years, males being affected equally with females   The total length of the history varied from one day to ten weeks and in no case was there any cyanosis at birth   The main clinical features were similar to those of the case here described, namely a fairly rapid onset of symptoms in a previously healthy child, beginning with fretfulness and refusal of food, then dyspnœa, and later cyanosis leading to a death not long delayed   In one of these cases there was a previous history of pneumonia, and cough was a prominent symptom in two   Neither clinically nor at autopsy did these cases suggest a congenital origin, and the features were more consistent with a past non-specific infection involving the heart

In other recorded cases it has been noticed that the symptoms dated from a severe lung infection (Mahon, 1936, and Lightwood and Court, 1939)   In the three cases reported by Neely (1941) the hypertrophy was attributed to an interstitial pneumonitis demonstrated at autopsy   It is interesting that the histological findings in the heart were similar to those mentioned above, the hypertrophy and endocardial thickening, however, being right-sided instead of mainly left-sided, possibly due to increased resistance in the pulmonary circulation

In one case with a mild degree of coarctation of the aorta, on the other hand, where the cardiac enlargement was considered to be much greater than could be accounted for by this lesion alone, the endocardial thickening was almost entirely left-sided (Levine, 1934)   The suggestion of increased resistance in the circulation playing a part in the ætiology has also been put forward by Powers and Le Compte (1938), whose case of a child aged eight months showed enlargement of the left ventricle, apparently almost entirely due to fibrous tissue, as there was no hypertrophy of individual muscle fibres and no evidence of hyperplasia   In cases of hypertension, however, no such endocardial thickening is found

Glycogen disease has undoubtedly been responsible for some of the reported instances of so-called idiopathic hypertrophy (Ellis, 1935), and only during the last few years has evidence of infiltration with glycogen been looked for post-mortem in such cases

A specimen of heart muscle from a case described by Carrington and Krumbhaar in 1924 was re-examined after being kept in formalin for many years, when special staining revealed the pressure of glycogen infiltration (Finklestein, 1936)   It is possible, in view of the fact that the glycogen is not uniformly distributed throughout the cardiac muscle but only in certain

areas (glycogenica circumscripta) that the condition is a more frequent cause than is at present realized (van Creveld and van der Linde, 1939)

In our case the main clinical features are typical of the majority of cases of idiopathic hypertrophy reported, except that the age of onset is slightly above the average.

Glycogen disease, vitamin B_1 deficiency, hypertension, gross anæmia, and congenital structural abnormalities were all excluded, and the ætiology of the condition of gross cardiac hypertrophy with endocardial and myocardial fibrosis as the main post-mortem finding, remains unexplained

SUMMARY

A case of cardiac hypertrophy in a child of two and a half years is described, and the steps taken to exclude the known causes of enlargement, including glycogen disease, are recorded

At autopsy the heart was found to be 290 g , which is almost of adult size, it showed no structural congenital abnormalities but a marked endocardial fibrosis which penetrated into the myocardium   Cases of a similar nature and some suggestions which have been put forward as to the cause of the condition are discussed

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Fig 1 —Teleradiogram of the heart two weeks after admission, showing gross enlargement of the heart to the left and upwards, and some increase in the root shadows
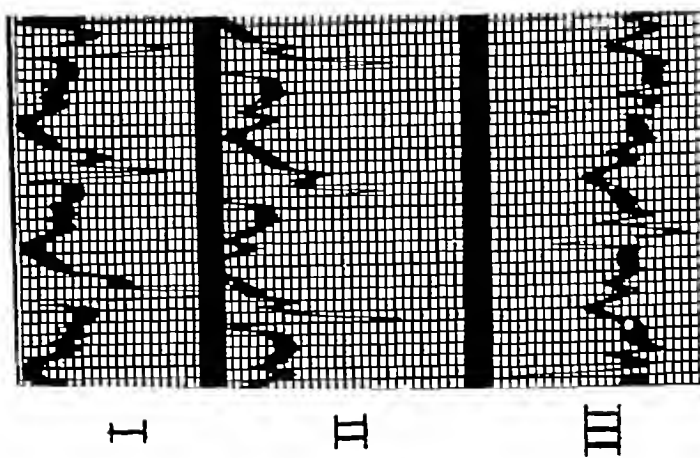
Fig 2 —Electrocardiogram taken two days after admission, showing right axis deviation with a wide notched QRS complex

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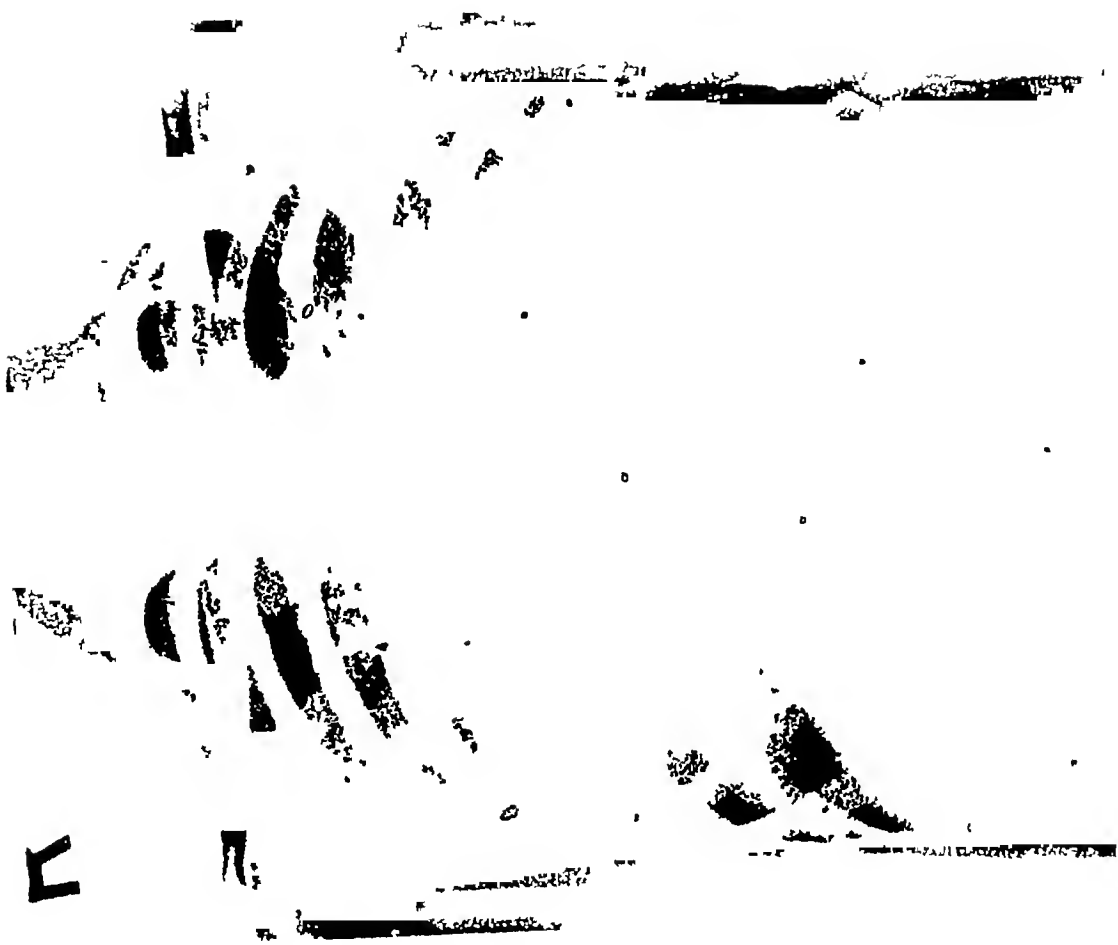
FIG 3 —Tcleradiogram of the heart seven weeks after admission showing no further increase in size but some shifting of the heart to the right with a considerable increase in congestion of the lung fields on both sides, and some blurring of the outline of the heart

FIG 4 —Section of endocardium of the left ventricle, the dark staining parts being fibrous tissue (van Gieson) Magnification 46

(A) indicates myocardium showing fibrosis

(B) indicates endocardium with gross fibrous thickening

THE HEART IN SCLERODERMA

BY

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The following case is of such rarity as to be worth recording in some detail   Although generalized scleroderma, itself a rare disease, may on occasion involve the heart muscle even if only microscopically, a careful search has shown that only nine examples have been recorded in which the cardiac lesion was gross and directly responsible for death from heart failure The rarity of this condition is shown by the fact that Weiss (1939) in an article on diseases of the heart and aorta that are not well recognized, in which he described some fifty rare conditions involving the heart, made no mention of scleroderma   In a later paper Weiss *et al* (1943) recorded nine cases of scleroderma with cardiac involvement, six of which died with generalized congestion   In three of them the cardiac symptoms preceded the skin changes by two years   Among a series of cases which Brock (1934) analysed in an attempt to draw a distinction between dermatomyositis and scleroderma, there was one in which the cause of death was heart failure   Heine (1926) also recorded such a case, and, more recently, Mathisen and Palmer (1947) have published details of one

CASE REPORT

The patient, a captain in the Merchant Navy, aged 49, stated that since about October 1945 he had noticed his hands and feet had become numb and white on exposure to cold, but quickly improving with warmth   There had been also a very gradual onset, of indefinite date, of muscular weakness and stiffness of his joints, which by May 1946 had become quite noticeable   The weakness was first noticed in the muscles of the calf of the left leg on climbing ladders on board ship, and progressed without remissions to involve successively the thighs, forearms, neck, trunk, and abdomen, till finally he found his jaws became tired when chewing and he would have to pause with food held in his mouth

At about the time the weakness became pronounced, he began to experience dyspnœa on exertion and swelling of the ankles, and three months later he noticed a sensation of retrosternal constriction, which was brought on by effort and also occurred while in bed at night The pain on effort was relieved immediately by rest and the pain at rest was relieved by drinking water   He experienced a severe attack of " indigestion " in May 1946   He estimated that he had lost at least two and a half stone in the past year

Apart from pneumonia in 1931, and in the same year a severe attack of seborrhœic dermatitis, which recurred mildly from time to time especially in hot weather, there was nothing of note in the past history   He had never been frostbitten, had served in the Merchant Navy since 1913, smoked twenty cigarettes a day, and drank moderately

There was nothing relevant in his family history

Physical Examination   When first seen early in August 1946 he was of good physique but still somewhat over weight in spite of his loss   The face was blank and remarkably expressionless   The skin looked smooth and shiny with an ivory pallor, the creases were ironed out, the lips were rigid   The facial movements were small and slow and seemed to be made with effort because of the thickening of the skin

N*   167

Examination of the cardiovascular system revealed that the heart sounds were distant, the rhythm was regular, the rate was 60, and no murmurs could be detected   There was no jugular engorgement   A small sacral pad of œdema was present   The blood pressure was 120/78   A skiagram of the heart showed a progressive generalized enlargement, particularly of the left ventricle (Fig 2, see p 171)   In an electrocardiogram on August 20, the P–R interval was prolonged to 0 28 sec, left axis deviation was present, the QRS complex was a little widened and slurred, T 1 was low, and there was slight depression of the S–T segment in lead IVF   An occasional auricular premature beat was present (Fig 1A)   The respiratory system and central nervous system were normal

The abdominal wall was remarkably thick so as to give an effect like orange peel, and firm pressure only could produce pitting, which filled up slowly   Neither the spleen nor liver could be felt   The muscles of the anterior abdominal wall were so weak that the patient was unable to sit upright without pulling himself up with his arms   All movements of the arms were weak, and he could not raise them to the back of his head without working his fingers along his temples   Extension of the elbows was limited to 10 degrees, but flexion was unimpaired   All movements of the wrists and small joints of the hands were limited   The skin and subcutaneous tissue were thickened and inelastic, almost brawny in feel, and this was more obvious towards the forearms and fingers, the hands showing the typical appearance of sclerodactyly   The legs showed changes similar to those in the arms   Pulsation in the dorsalis pedis artery was palpable in both feet   The upper edge of the trapezius muscle on both sides was strikingly hard and fixed, resulting in a " hide-bound " effect, feeling almost as though it were carved out of wood

Progress   On August 26, 1946, he developed suddenly an acute attack of urticaria with much swelling which involved the scalp, face, shoulders, and flexures of the forearm   A papular element appeared and became pustular in the beard area   Four days later gallop rhythm of the left ventricular type was noticed, his lumbar œdema increased, the œdema spread from his legs to his thighs, scrotum, and abdominal wall, and fine moist râles appeared at both lung bases   It was evident that heart failure was coming on rapidly   Bradycardia with frequent extrasystoles and occasional coupling then appeared and persisted in spite of discontinuing digitalis, the pulse falling to 46 and the auricular beat being audible at times   Partial heart block with dropped beats was, therefore, present   By September 16 complete heart block was present, and further flattening of T I and T II had occurred and T IVF had become inverted   Left ventricular premature beats were present (Fig IB)   On October 14, the pattern was much the same   Complete heart block persisted until death

During September his urinary output fell and the response to neptal was poor   He was given a neutral diet with low sodium intake and unrestricted fluids, and although his urinary output improved for a few days, he again developed oliguria   On September 30 he began to complain of dysphagia and this continued and became extreme just prior to his death   A fortnight before he died he developed a peculiar mental disturbance consisting of much depression during the day, mainly because he experienced some delay in remembering names of objects, and at night there was much talking and some shouting

On October 23 a second extremely acute exacerbation of the urticaria occurred and the patient presented an enormous " ballooned-up " appearance, resembling the famous advertisement for " Michelin " tyres   The urticarial rash became hæmorrhagic and serum exuded from the pressure areas and from many other minute excoriations on the trunk and legs   The rigid skin caused extreme pain and discomfort for it would hardly stretch to accommodate the œdema   Morphia scarcely gave any relief and he died the following day

Treatment   The urticarial attacks were treated with adrenalin and benadryl with no material effect   A penicillin course was tried but was also ineffective   Digitalis for his heart failure was disappointing, organic mercurial diuretics did not appreciably increase the urinary
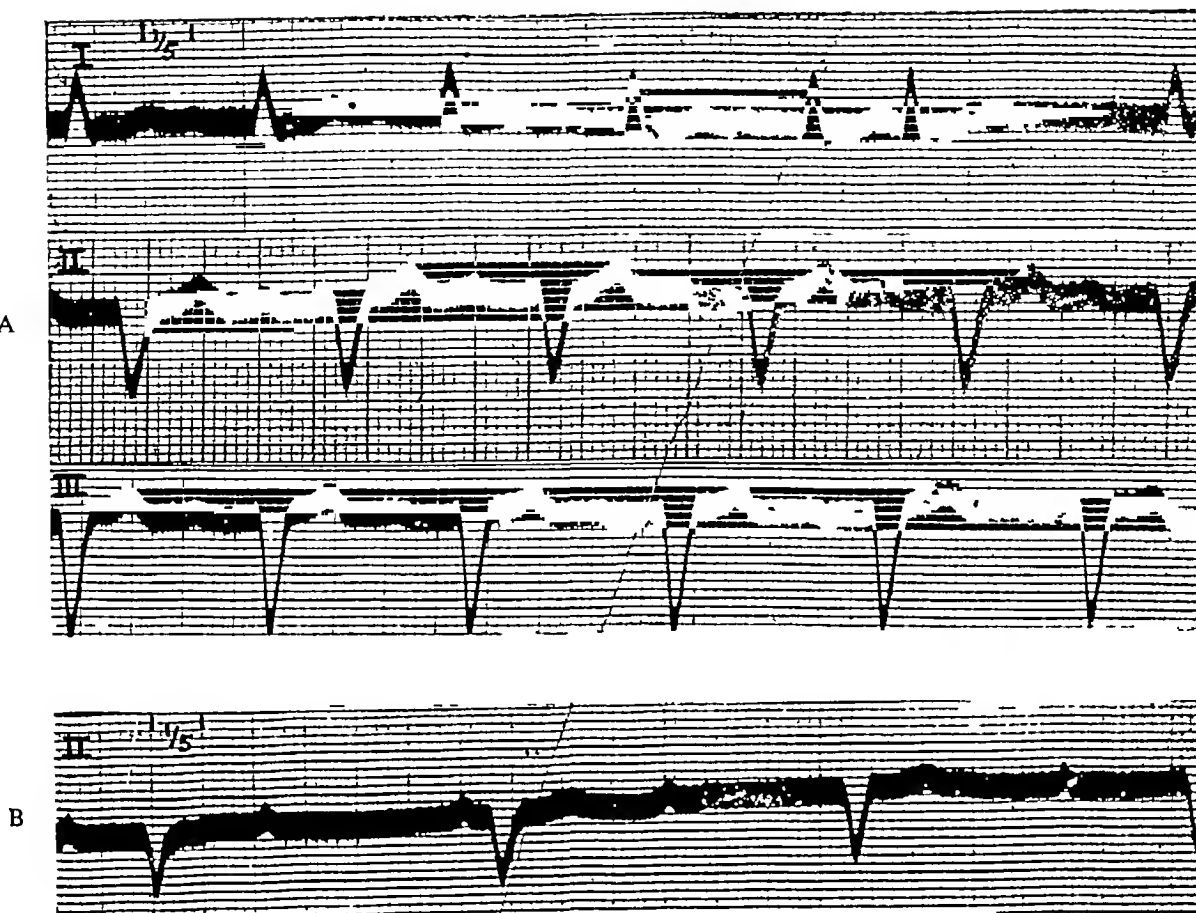
Fig 1 —(A) Electrocardiogram taken on 20/8/46 showing latent heart block
B) Electrocardiogram taken 16/9/46 showing complete heart block

volume, and although a neutral diet with a low sodium intake appeared at first to increase his urinary output, the effect was very short-lived

INVESTIGATIONS

Blood Counts These were repeated on several occasions and showed persistently a moderate polycythæmia and polymorphonuclear leucocytosis A typical count (August 19, 1946) was red blood corpuscles 7 56 million per c mm , hæmoglobin 130 per cent, white blood corpuscles 12,800 per c mm (polymorphs 78 per cent, metamyelocytes 6 per cent lymphocytes 11 per cent, eosinophils 3 per cent, mononuclears 2 per cent)

X-ray examination of œsophagus, stomach, and duodenum, and of forearms, legs, and thighs showed no abnormality

Chemical Investigations Fæcal fat estimation This showed, on repeated examination, an excess of unsplit fat, a typical result (September 17, 1946) being total fat 27 1 g per 100 g of dried fæces, split fat 7 2 g and unsplit fat 19 9 g per 100 g of dried fæces

Plasma proteins These were at first (August 10, 1946) normal—7 7 g per 100 ml and later (September 28, 1946) fell to 5 66 g per 100 ml , the albumen being 3 06 g and the globulin 2 60 g per 100 ml

Urinary creatinine This was persistently raised, for example on August 25–26, 1946, the total daily output was 1590 mg and preformed creatinine was 1010 mg

Serum calcium This was a little low—8 1 mg per 100 ml

Apart from the widespread and characteristic changes due to scleroderma described above there was much anasarca due to heart failure   Watery fluid streamed from the cuts   The skin, subcutaneous tissues, and the underlying muscles were very pale and indurated and cut as though the knife were blunt   The most striking changes were seen in the cardiovascular system   The heart was moderately enlarged (weight 370 g) and a small pericardial effusion was present   The ventricles were much dilated   The muscle looked pale brown and lacked resilience   The myocardium cut with the same resistance as the skeletal muscle, and the atrophied fibrous muscle presented an appearance which was striking and best described as " stringy "   The heart valves and coronary arteries were normal, and not affected by the fibrosis   The liver showed classical nutmeg changes, the spleen was indurated, cyanotic, and fibrous, and the kidneys were much swollen and indurated by passive congestion

Microscopic Findings   (Dr H A Magnus)   Pieces of tissue from all organs were sub-mitted for histological examination   All the endocrine glands were normal, except the testis which showed spermatogenesis arrested in the stage of spermiogenesis   The striking changes seen in the heart, subcutaneous tissue, striated and non-striated muscle will be described in detail, the other organs examined, including the pancreas, showed no unusual changes apart from congestion

Heart Muscle   Six blocks were sectioned from various parts of the heart   They all show a uniform histological picture   Scattered throughout are very numerous areas of fibrosis, the majority of these are small but just visible in the section with the aid of a hand-lens (Fig 3 and 4)   Each area of fibrosis has an irregular outline and the muscle fibres seem to taper away at the edge   Sometimes remains of isolated fibres can be seen in the centres of fibrotic patches   The heart muscle fibres show a considerable degree of brown atrophy, and collections of similar pigment are scattered about in the areas of fibrosis   All the small branches of the coronary vessels are quite healthy, in many areas there is an increased vascularity of the fibrous tissue (Fig 5)   There is no cellular infiltration of the heart apart from small numbers of eosinophils in the fibrous tissue   Sections impregnated by silver for reticular fibres show no new formation of fibrils in the scarred areas   Frozen sections stained by Sudan IV for fat show small quantities to be present in the muscle fibres

Skin and Subcutaneous Tissue   Apart from some vacuolation of cells the epidermis shows little change, but in all the sections examined there is a striking increase in the amount of collagenous tissue present in the corium   It extends from immediately beneath the epidermis to an average depth of 4 mm   The collagenous tissue is very dense and almost acellular, the blood vessels show no abnormality, the elastic tissue is still present but is fragmented (Fig 6)

Striated and Non-striated Muscle   The most severe changes are present in muscle from the abdominal wall and the forearm   Here the fibres are undergoing a form of coagulative necrosis   They vary greatly in size and shape, the majority have lost their striations and the cytoplasm is granular, in some areas the fibres have almost disappeared   The nuclei have either disappeared or have been exuded from the fibres   There is a remarkable absence of cellular infiltration in the interstitial tissue and in the sections examined there is no prolifera-tion of collagenous tissue between the muscle bundles   The blood vessels are normal (Fig 7 and 8)

Similar but less severe changes are present in the muscle of the tongue, pharynx, œsophagus, and intestinal wall

Scleroderma, if it is sufficiently generalized, may on rare occasions be associated with changes in the heart in some degree, but it is exceptional for these changes to be so great as to cause heart failure and death   Only nine such reported examples have been found
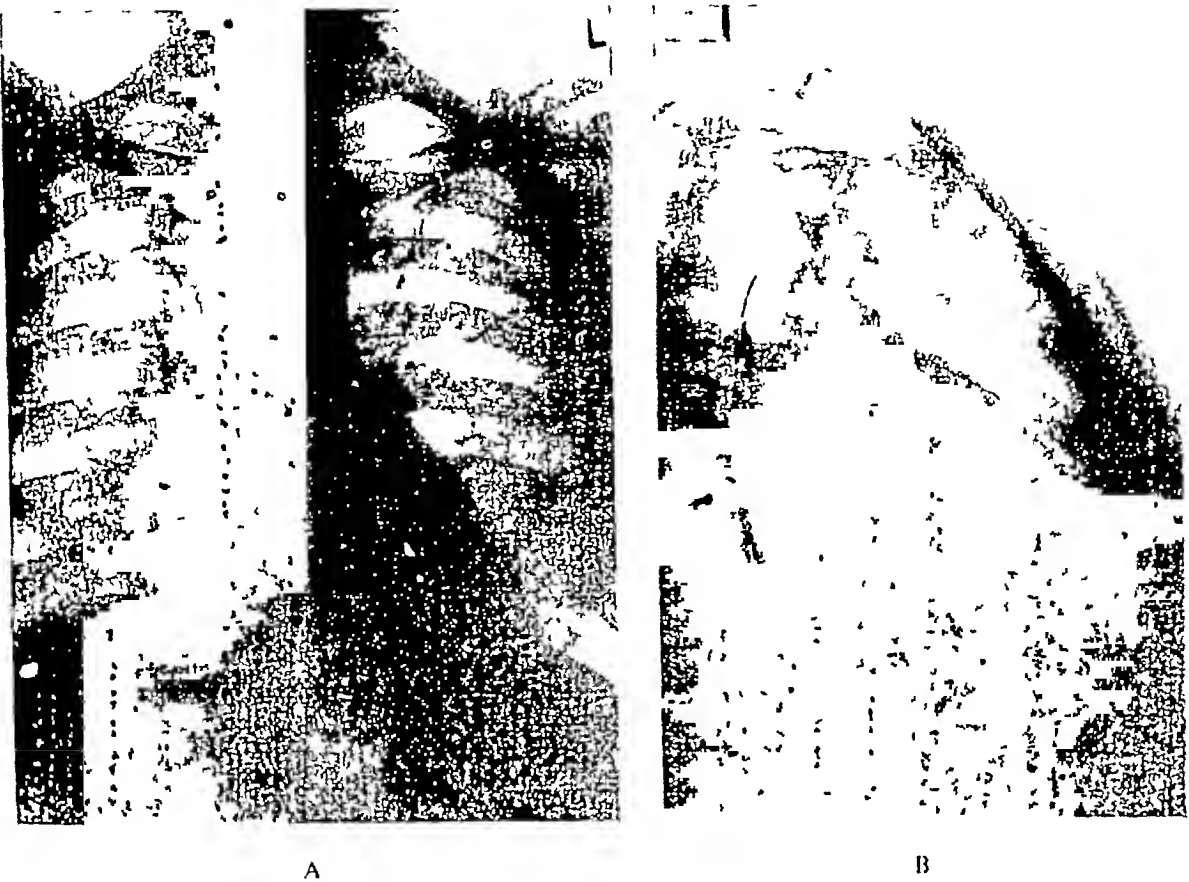
A B

Fig 2 (A) Postero-interior skiagram of the heart showing generalized enlargement particularly of the left ventricle
(B) Right oblique view
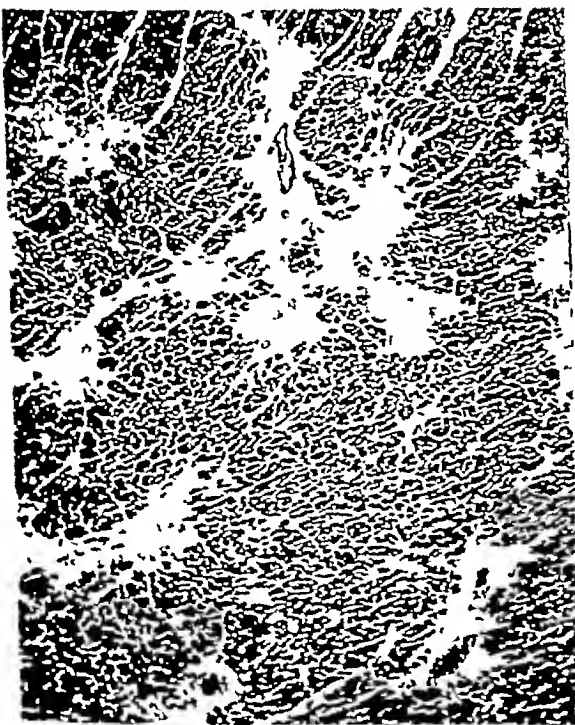
Fig 3 Fig 4

Fig 3 —A low-power view of the myocardium showing the numerous small scattered areas of fibrosis Hæma-toxylin and eosin Magnification × 24
Fig 4 —An area of fibrosis showing the irregularity of its edge and the absence of any inflammatory reaction Hæmatoxylin and eosin Magnification × 24
N**

FIG 5

FIG 6

FIG 5 —An area of collagenous tissue showing the well-developed blood supply Near the centre there are several isolated muscle fibres Hæmatoxylin and eosin Magnification ×55

FIG 6 —A low-power view cf skin and subcutaneous tissue showing the zone of dense fibrous tissue in the corium, and the absence of any cellular reaction Hæmatoxylin and van Gieson Magnification ×21
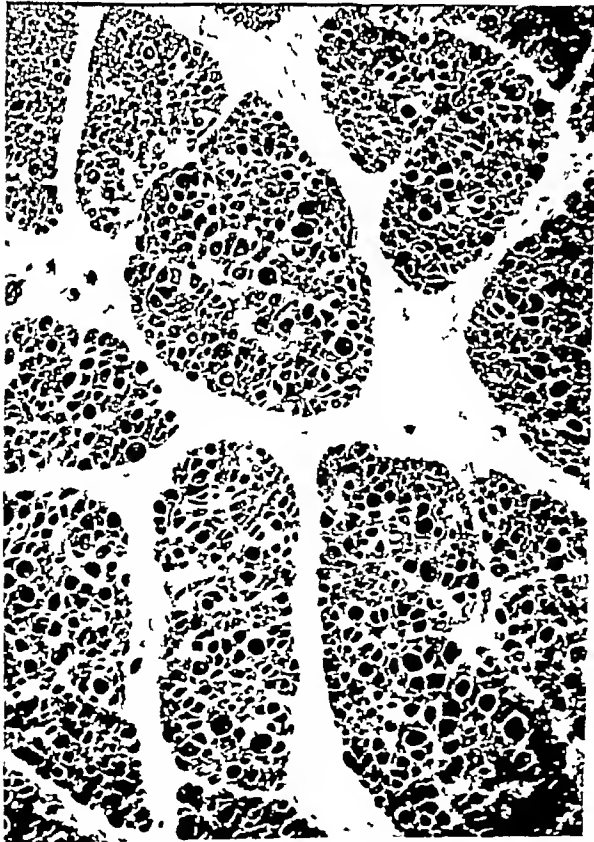
FIG 7

FIG 8

FIG 7 —A low-power view of part of a rectus abdominis muscle showing the great variation in the size of the fibres and the complete absence of cellular infiltration of the interstitial tissue Hæmatoxylin and eosin Magnification ×27
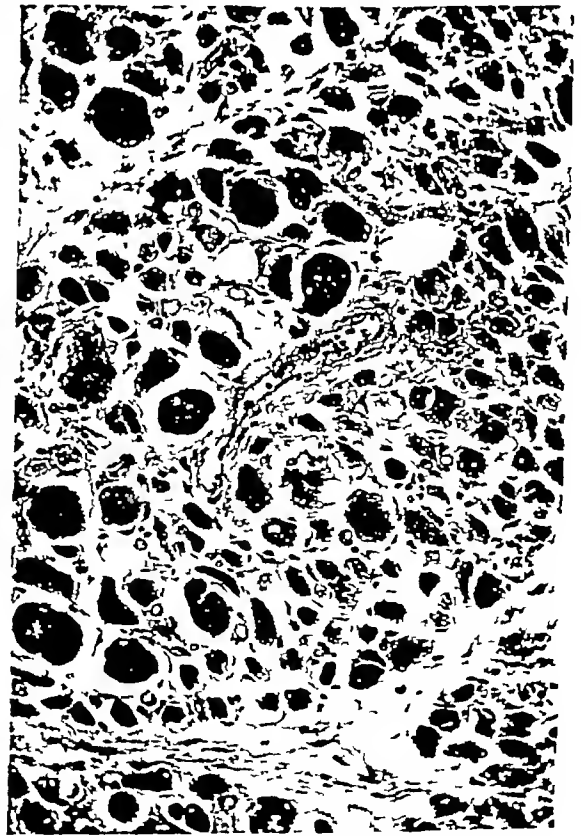
FIG 8 —A higher power view of a rectus abdominis muscle showing the structureless appearance of the muscle fibres many of which have almost disappeared. Hæmatoxylin and eosin Magnification ×63

The course of the disease is extremely variable It may be fulminating, with death resulting in a few weeks, or the progress may be extremely slow or remain stationary for years, death resulting from some other disease The case recorded died within a year of onset

The heart almost always fails with normal rhythm, auricular fibrillation having been recorded only once, by Weiss *et al* (1943) The picture which our case presented was of left-sided failure, accompanied by gallop rhythm, and gradually superseded by right-sided failure, and that is the usual one Some degree of heart block is common but this is the first example we can find of scleroderma progressing from partial heart block to complete heart block With such an interference with myocardial structure, the presence of heart block is not to be wondered at Considering the amount of cardiac muscle that was replaced by this peculiar fibrous tissue, and that the skin was also heavily infiltrated with it, it is rather surprising that the electrocardiogram deflections were of such good voltage In a case recorded by Petráček and Šilink (1937) there was simple bradycardia with a pulse rate of 54 a minute Weiss *et al* (1943) are of the opinion that the skiagram of the heart in these cases presents a suggestive triangular shape, somewhat resembling the shadow seen in pericardial effusion or sometimes in myxœdema, but the configuration of the heart in our case was in no way typical although there was some selective enlargement of the left ventricle The impression gained at autopsy, that the enlargement was due to dilatation and not hypertrophy, was borne out by the weight of the heart (370 g) No organic cause was discovered post-mortem for the dysphagia experienced by our patient, although cases have often been recorded where obstruction could be seen a few centimetres above the diaphragm It is tempting to presume that the obstruction was neurogenic in origin and that the sensation of præcordial constriction experienced by our patient was of œsophageal origin Certainly the coronary arteries were unaffected The patient of Mathisen and Palmer (1947) also experienced mild præcordial pain, which was relieved by rest, and this substernal tightness and constriction recurred a week prior to death and was more evident when she was excited Weiss *et al* (1943) consider that the pathological process consists essentially of a primary overgrowth of fibrous tissue, with secondary destruction of cardiac muscle fibres which are infiltrated and pushed aside, and Mathisen and Palmer (1947) also believe that the fibrotic areas encroach upon and destroy the adjacent myocardial fibres But from study of sections, we are of the opinion that, for some unknown reason, the cardiac muscle fibres disappear in patches and their place is filled up by this new tissue In Fig 7 and 8 it will be seen that many muscles fibre are structureless and disappearing, yet there is a complete absence of cellular infiltration of the interstitial tissue Our conception might be summarized by the title of one of Strauss's tone poems, namely " Death and Transfiguration " This interpretation of the histological picture would explain the complete absence of involvement of even the finest branches if the coronary vessels The significance of the polycythæmia, which was also present in the case recorded by Petráček and Šilink (1937) but in none of the cases of Weiss *et al* (1943), is not clear Possibly anoxæmia might have arisen as a result of the fixity of the thoracic cage which was present cases have been recorded with radiological evidence of involvement of the lungs, for example that of Mathisen and Palmer (1947), but in our patient the lung fields were clear

Treatment of the cardiac failure was disappointing, as might be expected from the nature of the process The presence of excess unsplit fat in the fæces suggested that the pancreas was affected This biochemical finding has been noted by other observers, and Sellei (1934) has recommended raw pancreas by mouth to alleviate the condition This was administered to our patient but without effect microscopically there was no evidence of pancreatic involvement

SUMMARY

A case of generalized scleroderma is described in which the degree of involvement of the

cardiac muscle was so great as to produce complete heart block and to be directly responsible for death from heart failure   The few other reported cases are reviewed

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TESTICULAR TERATOMA WITH EXTENSIVE INTRACARDIAC METASTASES

BY

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Patients suffering from malignant disease rarely die as a result of metastatic involvement of the heart, and the following unusual case is, therefore, recorded

CASE REPORT

The patient, a male aged 24 years, was admitted to hospital on March 14, 1946

History On February 22, 1946, he had acute pain in the left loin accompanied by malaise, sweating, headaches, pain in the chest, and cough with a small quantity of grey, watery sputum On March 10, his urine was noticed to have a dark colour On March 12, he had an attack of blurred vision lasting one day, his face became swollen, and vomiting commenced These symptoms were still present on admission to hospital by which time suppression of urine had been present for more than twelve hours

Examination The patient was alert, co-operative, and well nourished Pulse regular, small, rate 116 Temperature 97 2° F Respiration rate 30 The sclerae were faintly icteric, and there was generalized swelling and cyanosis of the face and neck Dilated veins were visible bilaterally running from the thoracic inlet down the arms in the region of the delto-pectoral grooves, but no cervical venous dilatation was noticed The chest was emphysematous The trachea was central Respiratory movements were poor but symmetrical on the two sides A few high-pitched rhonchi were audible, uniformly distributed over the lung fields The cardiac impulse was impalpable and the area of cardiac dullness reduced The heart sounds were faint but otherwise normal, and there were no bruits The liver was firm, smooth, not tender, and its lower border was palpable four fingers' breadth below the costal margin A firm fixed mass was palpable deep in the left hypochondrium extending down into the left flank and upwards towards the region of the spleen Localized tenderness was present over a point in the left sacrospinalis two inches above the level of the iliac crest Slight pitting œdema was present over both ankles The urine was a dark brown colour, odourless, and acid in reaction, with a specific gravity of 1030, it contained albumin, bile pigments, and urobilin

On the morning after admission the sclerae were more intensely icteric and a subconjunctival hæmatoma was present in the left eye Oedema and cyanosis of the head and neck were more intense and a petechial eruption was present over these areas On the basis of the above findings the patient was considered to have obstruction of both superior and inferior venæ cavæ Radiographs of the chest showed a pericardial effusion Paracentesis pericardii was performed and 750 ml of icteric serous fluid withdrawn This had little effect on the condition of the patient who was restless and, at time, irrational On the morning of March 15, he had an exacerbation of dyspnœa and cyanosis lasting about 3 hours At 5 p m on the same day, his symptoms again increased and by 7 p m he was severely dyspnœic and

cyanosed, pulse small, regular, rate 180, respiration 40   Pulsus paradoxus, which had been well marked after paracentesis, was no longer perceptible   The X-ray appearance was unchanged   A further paracentesis was attempted but had to be abandoned on account of the patient becoming severely distressed   His face and neck became almost black from cyanosis, and he died shortly afterwards

The turbid serous fluid withdrawn from the pericardium contained large deeply staining cells, some of which were binucleate, together with erythrocytes, lymphocytes, and a few polymorphs   It contained 0 8 g protein per 100 ml   Total leucocytes, 15,000, polymorphs 13,120 per c mm   Blood van den Bergh gave an immediate direct reaction, with total circulating bilirubin of 5 mg per 100 ml   Blood W R negative   Electrocardiograms showed slight right axis deviation

Post-mortem Examination

The body of a well-developed, well-nourished muscular young man   The skin showed slight icterus, and the head, neck and upper limbs were livid

The air passages contained frothy serous fluid   There were 300 ml of clear fluid in the right pleural cavity and traces of blood-stained fluid in the left   The lungs showed terminal congestion and œdema, no macroscopic deposits of growth were visible

The pericardium contained about 150 ml of turbid effusion, and showed fibrinous pericarditis   The heart was enlarged   Both right auricle and ventricle were dilated, and the former appeared, on external examination, to be entirely solid   On opening the heart, the cavity of the right auricle was found to be occupied by a huge cauliflower-like mass of growth which was obstructing the orifices of the superior and inferior venæ cavæ   The growth appeared to spring from the wall of the auricular appendix, the whole thickness of which was infiltrated by growth   The tumour protruded through the tricuspid orifice and a further discrete pedunculated mass sprouted from the wall of the right ventricle (Fig 1)   The myocardium was normal except where infiltrated by growth   The valves were normal

The liver was enlarged and showed gross venous congestion   The peritoneum was diffusely studded with minute petechial hæmorrhages, and a slight excess of free fluid was present

A large lobulated mass of growth was present in the lumbar lymphatic glands on the left side   The mass was firmly adherent to the front of the vertebral column and to the left psoas muscle   On section the tumour mass was found to be intersected by bands of fibrous tissue   The cut surface had a variegated appearance suggestive of a solid teratoma, and some compartments of the tumour contained material of a sebaceous consistency   This mass was quite separate from the kidneys and suprarenals   There was a small hydrocele of left tunica vaginalis   The testes were apparently normal on palpation and inspection, but section showed a small nodule 0 5 cm in diameter in the centre of the body of the left testis

Histology Sections of nodules in the testis showed malignant teratoma   The mixed nature of the growth was more apparent in the secondary deposits in lumbar glands and heart (Fig 2), in the latter much of the growth was necrotic (Fig 3 and 4)

COMMENT

There was nothing in the patient's history to indicate myocardial failure or the pericardial effusion as the prime cause of the clinical manifestations   They were adequately explained by the necropsy finding of a large tumour arising from the wall of the right auricular appendix and almost completely occluding the auricular cavity

In order to obstruct the flow of blood from both venæ cavæ, a tumour must almost completely fill the auricle, so that signs of caval obstruction will be unlikely to appear until a short

time before death, as happened in this case Œdema of the face from obstruction of the superior vena cava was among the early presenting symptoms, while hepatomegaly was not noticed until the patient's admission to hospital The liver enlarges rapidly in response to back pressure along the inferior vena cava, whereas a longer time is required for anoxia and local nervous mechanisms to produce manifest œdema It would appear that obstruction of the superior vena cava was present from the onset of the illness, whereas obstruction of the inferior vena cava occurred relatively late, death intervening before there was time for œdema of the lower extremities to develop

The purely right-sided situation of the lesion explains the relatively mild degree of respiratory distress despite progressive systemic venous congestion and cyanosis The acute terminal episode was presumably due to impaction of the mobile portion of the growth in the tricuspid orifice producing complete circulatory obstruction, and a temporary or partial obstruction probably caused the sudden transient increase of symptoms twelve hours before death It is interesting to compare the results of rapidly progressing right auricular obstruction with those of a similar left-sided lesion Fawcett and Ward (1939) describe a case with ten months' progressive dyspnœa, cough, and præcordial pain, presenting attacks of faintness and dizziness due to a pedunculated tumour of the left auricle Wainwright (1938) records cases of both left- and right-sided occlusion Other examples will be found in the list of references given below

Yater (1931) lists the " ball valve " type among his anatomical classification of heart tumours Yater (1931), Fishberg (1930), Lisa *et al* (1941), and Doane and Pressman (1942) all stress the frequency of sudden death, which may be the first indication of the presence of cardiac tumour

The post-mortem findings suggest that lymphatic spread occurred early to the para-aortic glands around the renal artery Thence malignant emboli obtained entrance to the venous blood stream via the cisterna chyli and thoracic duct, there being no macroscopic evidence of the invasion of the inferior vena cava or its tributaries, such as was found in cases of blood-borne tumours of the right auricle described by Paget (1855), Kanthak and Pigg (1897), Parkes-Weber (1915), French (1912), and Fry and Shattock (1926)

The intracardiac metastases probably arose by direct implantation of cells in the wall of the right auricular appendix Evidence for this is as follows—(1) this region of the auricular wall showed maximal infiltration by malignant cells, elsewhere the cauliflower-like mass lay free in the auricular cavity, following the direction of blood flow through the tricuspid orifice and allowing blood to pass between it and the auricular wall, (2) the tendency towards stasis is maximal in this part of the right auricle as shown by the tendency for ante-mortem thrombi to form here in cases of auricular fibrillation, (3) the absence of pulmonary metastases, (4) the absence of arrhythmia indicating that the sino-auricular node and bundle of His were free from infiltration Pericardial effusion occurring without obvious cause is a frequent manifestation of a tumour of the heart (Yater, 1931)

Summary

A case of extensive intracardiac metastases from a clinically undetectable testicular teratoma is recorded The clinical picture is discussed in the light of the autopsy findings and with reference to similar reported cases

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Fig 1 —Heart with right cavities opened, showing occlusion
of right auricle by friable tumour, and discrete nodule
of growth springing from wall of right ventricle

Fig 2 —Section of lumbar tumour showing epidermal elements   Magnification   120

Fig. 1   Section of intra auricular tumour showing extensive areas of necrosis and hemorrhage   Magnification   × 32

ERGOTAMINE AND APPARENT CORONARY INSUFFICIENCY

BY

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Since 1942 we have used hypoxæmia tests (Nylin, 1944) as a routine in the clinical examination of patients complaining of symptoms of coronary insufficiency   The results from the first three years' material were reported in this journal (Biörck, 1946)   A larger material was investigated (Biörck and Pannier, 1946), and this survey established that the test did not only disclose latent coronary insufficiency in many cases with suspected organic coronary heart disease (" coronary sclerosis ") but also produced apparently pathological electrocardiograms in patients with symptoms of cardiac neurosis in whom there was, on account of their age, very little reason to suspect organic changes in the coronary circulation   The study revealed a relative predominance of women among those who showed a positive hypoxæmia test, and the younger the age group the greater was that relative predominance   There was also a number of cases, mostly women, where the history and the general impression of the patient were suggestive of cardiac or general neurosis

This impression led us earlier to try to counteract the nervous factors and thus obtain cardiograms that would be less affected by a nervous component   In one case of a possibly climacteric depression we succeeded in abolishing the induced cardiographic changes suggestive of coronary insufficiency by previous injection of morphine-scopolamine

In a recent investigation Lindgren (1946) has shown that the effect of hypoxæmia on the cardiogram can be diminished in some cases of angina pectoris of the organic type, when the patient has previously received a local anæsthetic at the area of referred pain   This will probably signify that the pain itself, in some instances, induces a vicious circle, and that there is a functional component superimposed upon the organic one, even in cases with true coronary sclerosis

Although as yet nothing seems to be quite certain regarding the innervation of the coronary vessels (Katz and Jochim, 1939), it may be that both the vagi and the sympathetic carry constrictor and dilator fibres, the distribution of which may be subject to great individual variations   Blocking of the sympathetic was nevertheless regarded as one possible way of studying the problem of the importance of functional factors in some cases of unexpected positive hypoxæmia tests   Nordenfelt (1941) has clearly demonstrated the effect of ergotamine in cases of increased tonus of the sympathetic   cardiograms that suggested coronary insufficiency could in several instances be transformed into normal curves by means of ergotamine, 0 5 mg intravenously or subcutaneously   These findings have been verified by us in a number of cases

The cardiographic findings in the hypoxæmia test are usually ascribed to the induced anoxæmia or ischæmia of the myocardium   The degree of myocardial anoxæmia is due to a number of factors such as   ventilation, arterial oxygen tension, and arterial pH, as recently shown by Christensen (1947) and Malmström (1947)   The findings of Mainzer and Krause (1939) and of Biörck and Pannier (1946) do, however, point to further factors, among which

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hormonal influences, reflex mechanisms, and possibly intermediary tissue metabolism should be considered   This study deals with one of these factors—the sympathetic nervous influence It has hitherto not been possible for us to carry out determinations of ventilation, arterial oxygen tension, and the pH of the blood in these cases, and it may be argued that the positive

TABLE I

CLINICAL FINDINGS IN THE TEN PATIENTS

Case No	Sex and Age	Diagnosis	Blood Pressure	Sedim rate	B M R	Hæmoglobin %	Organic heart disease *	Neurosis
1	m 14	Vegetative instability	130/70	1	−2	92	?	?
2	m 20	Cardiac neurosis? Acute myocarditis?	130/90	1	+4	76	?	yes
3	f 26	Psychopathia	140/80	3	+7	78	?	yes
4	f 26	CO - intoxication Myocardial damage?	110/60	8	+8	78	.? *	?
5	f 26	Cardiac neurosis?	110/80	6	−5	71	?	?
6	f 26	Cardiac neurosis?	140/70	12	—	80	?	?
7	m 28	Benzol intoxication Neurosis	130/85	4	—	82	? *	yes
8	f 29	Hypercholesterolæmia + Coronary heart disease?	135/80	8	−7	73	yes ?	?
9	m 35	Subchronic myocarditis?	135/80	17	−2	78	yes ?	yes
10	f 53	Spondylosis + neurosis + coronary heart disease?	150/100	3	—	77	?	yes

* The electrocardiogram was normal in each case, except that in Case 4 there was a suggestion of myocardial damage or of sympatheticotonia and in Case 7 of vagotonia

TABLE II

ELECTROCARDIOGRAPHIC FINDINGS BEFORE AND AFTER ERGOTAMINE

Case No	Original hypoxæmia test			Hypoxæmia test after ergotamine			
	Electrocardiogram		Increase in heart rate percentage	Electrocardiogram			Increase in heart rate percentage
	At rest	Hypoxæmia test		At rest	20 min after ergotamine	Hypoxæmia test	
1	normal	positive	40	normal	the same	negative	33
2	normal	positive	30	normal	the same	negative	45
3	normal	positive	33	normal	the same	negative	4
4	normal	positive	33	normal	the same	negative	7
5	normal	positive	50	normal	the same	negative	45
6	normal	positive	50	normal	the same	negative	25
7	normal	positive	50	normal	the same	negative	33
8	normal	positive	40	normal	slightly improved	positive	75
9	normal	positive	15	normal	slightly improved	negative	30
10	normal	positive	60	normal	slightly improved	negative	50

" Normal " denotes an essentially normal curve
The increase in heart rate in the hypoxæmia test at the ergotamine test refers to the curve after ergotamine, not to the curve at rest before ergotamine
The expression " improved " refers to changes in the shape of the cardiogram within the normal limits

hypoxæmia tests have been due in all cases to hyperventilation. Although this may have been the cause in some instances it is hard to see how ergotamine could abolish this effect

The material comprises 10 cases, 4 men and 6 women. Most of them were rather young. Two of them had a slight tendency towards transient hypertension, otherwise there was none with evidence of organic heart disease. Most of them were neurotic or showed a vegetative lability (see Table I). They were submitted to routine cardiographic examination and recommended hypoxæmia tests. Apart from one case (Case 4), whose cardiogram was earlier regarded as indicating either myocarditis or sympatheticotonia, all the curves were normal

The hypoxæmia test was performed with 9 per cent oxygen in nitrogen for 10 minutes and evaluated according to the criteria of Levy *et al* (1941). These 10 cases were selected for ergotamine-hypoxæmia on account of the apparent discrepancy between the age or the history and the result of the test. They were all re-examined with regard to their circulatory system before the procedure, because of the danger of unfavourable reactions, if the patient should have an organic lesion of the coronary arteries (Lindgren, 1947). Only in one case did we encounter any complication with the ergotamine, probably on account of injection into a nerve

The interval between the first hypoxæmia test and the one with ergotamine has varied from a few days to one month. However, in no case has there been any change in the patient's condition, subjectively or objectively or any special treatment. The cardiogram at rest has in all cases remained essentially the same

The ergotamine hypoxæmia test has been performed as follows. After a previous curve at rest the patient has been given ergotamine 0 5 mg (Gynergen, Sandoz) intramuscularly or subcutaneously. After 20 minutes a new cardiogram has been taken, after which the hypoxæmia test has started. After 10 minutes a third curve has been taken and the patient given 100 per cent oxygen to breath. Two examples are given in Fig 1 and 2

The results of each case are shown in Table II. Out of ten cases not less than nine have shown a negative test after ergotamine. This naturally does not mean that there is no change at all, but the changes are within the limits according to Levy's criteria. The one (Case 8), that remained positive, suffers from a moderate cholesterolæmia and has a family history with several deaths from cardiovascular sclerosis in the fourth decade

The investigation has given some further evidence in favour of the view that nervous influence, presumably over-activity of the sympathetic which is not uncommon in young people, may give a positive hypoxæmia test. The factors that cause positive results can be

FIG 1 —Electrocardiograms from Case 1, a boy aged 14, with vegetative instability
(A) At rest   (B) After ten minutes' hypoxæmia   (C) At rest on a later date   (D) Twenty minutes after 0·5 mg. ergotamine   (E) After ten minutes' hypoxæmia.
The five electrocardiograms are in each case I, II, III, and the anterior and posterior chest leads according to Nylin-Nehb
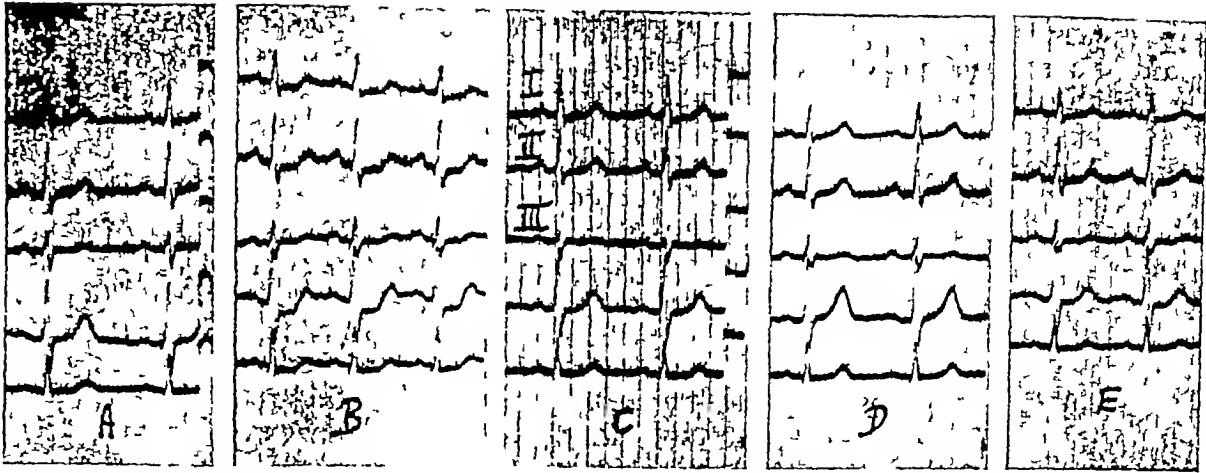
FIG 2 —Electrocardiograms from Case 2, a woman aged 26 years, with a probable cardiac neurosis (A)–(E) as for Fig. 1

partly paralysed by blocking the sympathetic with ergotamine Endogenous changes in vegetative tonus may naturally also be one explanation This may express itself also on the ventilation, which should, therefore, if possible, be studied together with the drug action This study does not attempt to solve the problem of the vegetative activity on coronary circulation, but merely points to its existence and the possibilities of its clinical exploration

SUMMARY

In ten cases with positive hypoxæmia tests where it was questioned if the outcome of the test might not be due to " functional " factors rather than to coronary sclerosis or myocardial disease, a new hypoxæmia test was performed after the injection of ergotamine 0 5 mg In nine of the cases the test after ergotamine was negative This points to an effect of the sympathetic nervous system in such cases Further investigations are needed

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COARCTATION OF THE AORTA

BY

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The collateral circulation in the chest wall, when well-developed, may be the most striking feature of coarctation of the aorta   It was not, however, often recorded by the good clinicians of the past though they had a wide knowledge of the subject in the post-mortem room (Fawcett, 1905)   Coarctation is not very uncommon, as hospital post-mortem statistics show that it occurs in about one case in a thousand (Fawcett, 1905, and Evans, 1933, and Blackford, 1926) In spite of this it is still frequently missed probably because in many cases the collateral circulation is not as obvious as it is expected to be, and because the insistence of Lewis (1933) on the importance of the poor femoral pulse is still not remembered often enough

In infancy, it is rarely diagnosed in life, and in children less often than in adults though the number of reported cases is increasing   This is partly because the blood pressure does not rise greatly for some years and because the collateral circulation does not become evident in the thoracic wall till later   Sheldon (1945) states " a collateral circulation does not develop until about six or seven years of age, but before this the diagnosis can be made with assurance, in the presence of the other physical signs—raised blood pressure in the arms with no femoral pulse and a systolic murmur at the base of the heart "

Our main objects in this paper are to record the development of these changes in some young patients watched over several years, to describe a new sign for demonstrating the collateral circulation, to discuss some theoretical aspects, and to emphasize the points that we think likely to help in the diagnosis

The cardinal points in the diagnosis are

(1) A raised blood pressure in the upper half of the body
(2) Forcible pulsation of the arteries in the neck, sometimes simulating aortic incompetence, this was obvious in 12 of our 15 cases and was sometimes the first suggestion of any abnormality   it should direct attention to the high blood pressure in the arms when this has not been taken as a routine
(3) Feeble or absent pulsation in the femoral arteries and the abdominal aorta, and a low blood pressure in the legs with a high or relatively high pressure in the arms
(4) The collateral circulation shown round the scapulæ, on the side of the chest wall, and over the anterior abdominal wall
(5) The collateral circulation shown by notching of the ribs on X-ray examination
(6) A systolic murmur (rarely with a thrill) at the base of the heart and often in the back, sometimes with a diastolic murmur

The diagnosis is most likely to be made in the less obvious cases if the femoral pulse is felt for in every case with high blood pressure, or with obvious arterial pulsation in the neck, or with an unexplained systolic (or diastolic) murmur at the base of the heart   Although the femoral pulse is often difficult to feel, there are as a rule no symptoms of any gross circulatory deficiency in the legs because an adequate amount of blood flows in by devious channels in spite of the absence of a clear pulse wave transmitted directly to the femoral arteries   Symptoms of slight circulatory deficiency may be found on more careful questioning, especially

aching in the legs after marches or long walks   As soon as there is doubt about the femoral pulse the blood pressure should be taken in the legs

The collateral circulation will be considered first and then the notching of the ribs, next the size of the heart and the murmurs, next the blood pressure and such evidence as we have been able to obtain of the time of development of the rise of blood pressure, and finally the prognosis

The Collateral Circulation

We wish to describe a new sign for demonstrating this and to bring forward some evidence for the time and rate of the development of the superficial collateral circulation and also of the notching of the ribs from infancy to adult life   The collateral circulation was well studied by early workers and there is a model in the Guy's Hospital Museum from a specimen of Wilks dating from 1859   The subject has been fully reviewed by Bramwell and Jones (1941)

When the collateral circulation is not obvious inspection may fail to show the enlarged and tortuous arteries under the skin   The surface should be inspected from all angles in a good light and the hand passed lightly over all likely positions as in this way a small portion of a pulsating artery under the skin will sometimes be revealed   The patient should also be made to bend forward (see later)

The collateral circulation increases with the years, presumably till it reaches a balance with the demands being made on it   After surgical ligature of an artery the collateral circulation seems to reach its maximum within a relatively short period of months   The much longer period of development with coarctation of the aorta suggests that the need for it increases and this is probably mainly because the actual size of the coarctation does not increase in diameter at the same rate as the rest of the aorta, if at all, so that relatively the degree of stenosis increases until the age when full physical development has been completed

In all our patients observed over a period of several years increases in the collateral circulation as evidenced by the subcutaneous arteries were noted

Case 1, aged 7   It was visible and palpable, especially round the scapulæ, when he was first seen During the next three years it became more obvious, and still more so by the age of 13 when he was last seen

Case 2, aged 7   There was thought to be some increased arterial pulsation in the scapular regions when he was first seen, but it was indecisive   A year later it had increased and during the next three years it became more easily seen and more widely developed, and possibly again during the following three years, up to 14 years of age   Two years later it was not so easily seen, but this was due to an increase of weight and subcutaneous fat since he had been evacuated to the country   By 1947, when he was 21, it was easily seen both at the front and back of the chest and also on the upper abdomen above the umbilicus, and had increased in the last 4 years

Case 3, aged 25   No diagnosis was made at 25, but at 28 years there was an obvious collateral circulation over the abdomen and round the scapulæ   She was not seen again for 10 years and it was then extremely obvious in all these sites   It may be that the circulation was not looked for carefully enough when she was 25 but it certainly became more obvious between 28 and 39 years of age

Case 4, aged 17   The collateral circulation was already well developed   She died later that year

Case 5, aged 19   The collateral circulation was already easily seen and felt all over the back and up the abdominal wall where the arteries were unusually tortuous and pulsating   Ten years later, when he was 29, additional vessels were seen along both borders of the sternum   He himself thought they had become more visible during these last 10 years and were especially evident when he became heated

Case 6, aged 13   There were some enlarged arteries round the scapulæ, but they were not very obvious   When he was 22, it had increased and was seen in front along the borders of the sternum In addition, palpation revealed several vessels that were not visible

In most of these cases the collateral circulation became more obvious between childhood and adult life and in Case 3, rather surprisingly, it seemed to have increased between 25 and 39 years of age   An increase in weight with subcutaneous fat was important in hiding the collateral circulation and this should be remembered   A hot day or a hot room helped in making it more obvious

Where the collateral circulation was not very obvious it seemed most likely to be found in the scapular regions   In three (Cases 4, 11, and 13) it was palpable only in the scapular region, and generally palpation was a more sensitive method of detection than observation   In Case 9 the only sign of it that was noted was the notching of the ribs, but we would emphasize that the special method for demonstrating its presence was not used and we have not been able to get in touch with him again

A New Sign of Coarctation of the Aorta

When this paper had been nearly completed, one of us (S S) found that, by making the patient stoop or bend forward with the arms hanging by the side, collateral arteries under the skin of the back and sides of the thorax suddenly appeared where none were visible before

In two patients (Cases 14 and 15) no collateral arteries were visible on ordinary inspection, but on making them stoop forward, they at once became very prominent, and the diagnosis of coarctation could thus be made on this sign alone (see Fig 1)

So far the sign has been found in 7 of 8 cases tested and the others have not been available for re-examination   In Cases 2, 3, 5, 11, and 13, the collateral circulation could already be seen, sometimes easily, but it became more prominent on bending forward and became visible in fresh places where it had not been seen before (see Fig 2)

After the sign had been found positive in three consecutive cases it was hoped that it might be of general application, but in Case 6, where the collateral circulation could already be seen, bending forward did not seem to increase it in any way

Other changes of posture also caused the collateral arteries suddenly to appear or to increase their prominence, such as forward movements of the shoulders with the arms brought forward   Another good position is for the patient to lie prone on a couch with a cushion under his chest and the arms hanging down over the edge   But the optimum method is by stooping or bending forward with the arms hanging vertically

The reason for the sudden appearance of these arteries with this change of posture was rather puzzling at first   After discussion with Professor Whillis of the Anatomy Department, Guy's Hospital, he suggested that these particular movements simply widened the costo-clavicular space   It follows that in cases of coarctation where this sign is positive, there must in ordinary positions be a sufficiently narrow space between the clavicle and the first rib to produce some constriction and obstruction of the subclavian artery   Any movement that increases the costo-clavicular space will then relieve this partial obstruction of the subclavian and so the vessels having their origin from the partially constricted artery will suddenly fill up and become larger so that collateral branches previously invisible will become easily seen   Stretching of the skin or gravity or compression of the abdominal aorta do not cause the arteries to show up in this way

In coarctation of the aorta the subclavian artery is very often dilated and tortuous and so it is quite understandable that some partial compression would occur in the costo-clavicular space   In the cases that do not show this sign the space between the clavicle and the first rib is wide enough not to compress even the dilated subclavian artery   We do not think that compression by the other structures in the costo-clavicular space, such as the nerve plexus or the scalenus muscles, plays any important part

We have tried to get X-ray evidence for the widening of this space   It has been difficult to find a position where one can take X-ray pictures that will show the amount of widening of the space with the forward position of the shoulders, but we think that in one or two cases stereoscopic views have demonstrated this

Further evidence that the subclavian artery is partially compressed in the costo-clavicular space is provided by the increase of the radial pulse that follows forward movement of the shoulder or other movements that cause widening of the space

It is therefore advisable that in every suspected case of coarctation of the aorta, and even in many cases of high blood pressure, this sign should be looked for   The best position is with the patient stooping forward and with the arms hanging down vertically, and the back should then be examined in a good light   By this means we feel that fewer cases of coarctation will escape diagnosis

Notching of the Ribs

Notching or scalloping of the ribs is almost pathognomonic of coarctation of the aorta though we have seen one suggestive case lately where the diagnosis seems excluded   It was present in every one of our cases examined radiologically though the degree varied considerably In children it often has to be carefully looked for, as carefully as the collateral circulation, and in younger children it may be absent   Before 1946 we regarded it as perhaps the most decisive point in diagnosis, but increasing experience of feeling the femoral pulse makes us rank this as a more important sign because it can be found on clinical examination and because in children it is present from an earlier age

Fray (1930) in a note added to his paper says that in one of King's cases there was no visible rib-notching in two films taken when the patient was 10 and 12, but that it had started to show when he was 17 years of age   Brown (1939) states that the youngest recorded example of rib-notching was at 6 years of age   Reifenstein, Levine, and Gross (1947) in a paper dealing mainly with cases that had come to autopsy quote a case of Farris (1935) where there was slight rib-notching in a boy of 11 years, and add that Bland and also Sosman had informed them of cases where they had seen it rather earlier than this   They found it present in 75 per cent of the 43 cases where the information was provided, but in adult cases diagnosed clinically it seems to be present more often than this

In our Case 1 who was 7 when first seen it was slight but definite   In our Case 2 who was also 7, it was suspected but indefinite, one year later (1934) it could be clearly seen but was still slight (see Fig 3 and 4)   In the case of Rooke (1938), aged 3, there was no visible rib-notching although the collateral circulation was fairly well developed   Neuhauser (1946) has mentioned a case where it was said to be visible in an infant 9 months old, but the next youngest case referred to was 8 years old

Notching of the ribs obviously depends on the degree of dilatation and tortuosity of the intercostal arteries in their contact with the ribs   In all the 5 patients observed over a period of several years the degree of rib-notching increased   Sometimes the increase is only in the depth of the notching, but sometimes especially in the younger patients the number of ribs affected also increased considerably   The changes were greater in some than in others

Case 1, aged 7   Notching was slight but noticeable, at first in only 3 or 4 ribs   It had increased by the time he was 9, and again when he was 11 years old   When last seen, aged 13, it was still only moderate (see Fig 3)

Case 2, aged 7   Notching was suspected on careful searching, but was regarded as indecisive when he was first seen, though looking back at the film and comparing it with later ones it can be seen A year later it was still slight in degree but was now decisive (see Fig 4B), and after another three years there appeared to be a further increase   When he was 20, there seemed to have been a further increase from the age of 11, so that in this case the gradual erosion seems to have taken place over a period of many years (see Fig 4)   The number of ribs affected had also increased from 2 or 3 on one side in 1933 to 8 on both sides in 1947

Case 3, aged 25   The diagnosis was not made till she was 28, though the high blood pressure had been noted at 25   At 28, a suggestion of rib notching was reported, but unfortunately the X-ray film has been lost   Eleven years later, when she was 39, it was well marked in the first 3 ribs on both sides   Here the rib notching and the collateral circulation both seemed to have continued increasing till a later age after the blood pressure had become stabilized

Case 5, aged 19   This patient showed the least change, but all signs were well developed when he was first seen at the age of 19   Ten years later the notching was a little deeper in one rib and more clear-cut in another (see Fig 8)

A

B

FIG 1 —The collateral circulation demonstrated by bending forward, in Case 15   The picture in Case 14 was similar
(A) When standing upright, no collateral circulation could be seen even in a good light
(B) After bending forward the collateral circulation can easily be seen and there is one specially obvious artery on the right

C

B

A

Fig. 2.—The collateral circulation greatly increased by bending forward in Case 2 above and in Case 5 below. (A) When standing upright a few arteries of the collateral circulation can be seen. (B) After bending forward the number of visible arteries is greatly increased. (C) Bending forward a little less than in (B) to demonstrate the collateral circulation on the side of the chest.

Fig. 3 —The development of rib notching in Case 1

(A) When aged 7, showing visible but very slight notching. The blood pressure was 142/70 and there was aortic regurgitation.
(B) When aged 11, the notching of the ribs can be seen more easily, especially on the right side. The great increase in the size of the heart is due to an attack of rheumatic pericarditis from which he recovered but was left with further cardiac enlargement (see Table 1).
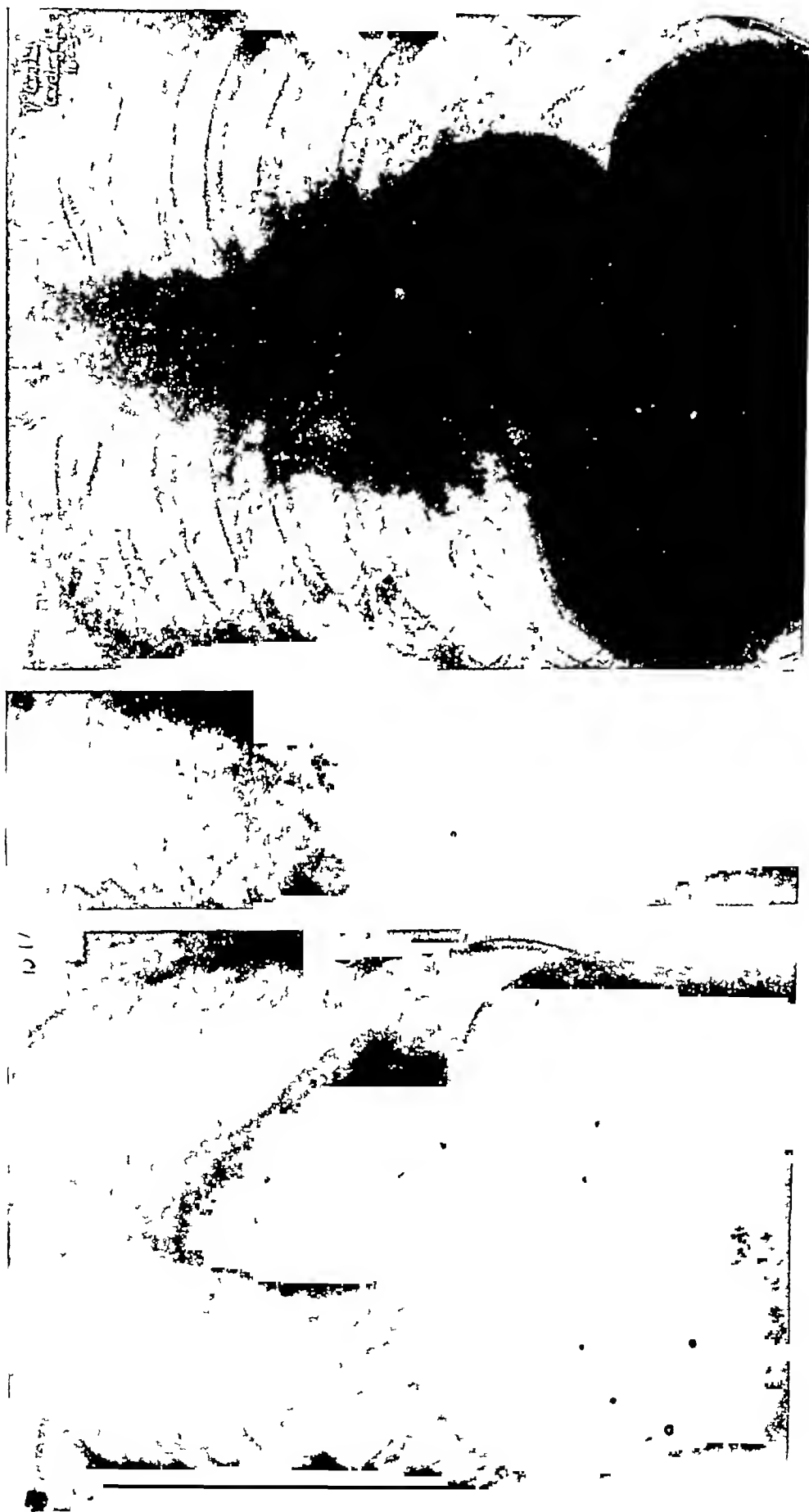
FIG 4 —The development of rib notching in Case 2

(A) When aged 7, showing no convincing notching, though it may be suspected
(B) After 17 months, the right side only, showing slight but decisive notching
(C) After 13 years showing increased notching of several ribs on the right and one large clear-cut notch on the left that could not be seen before   The heart has grown but has not increased relatively to the chest

B

A) Case 6, aged 22, with no aortic diastolic murmur and a B.P. 200/85   (B) Case 13, aged 27, with a B.P. 190/100 (165/92 after resting in bed) and no aortic diastolic murmur
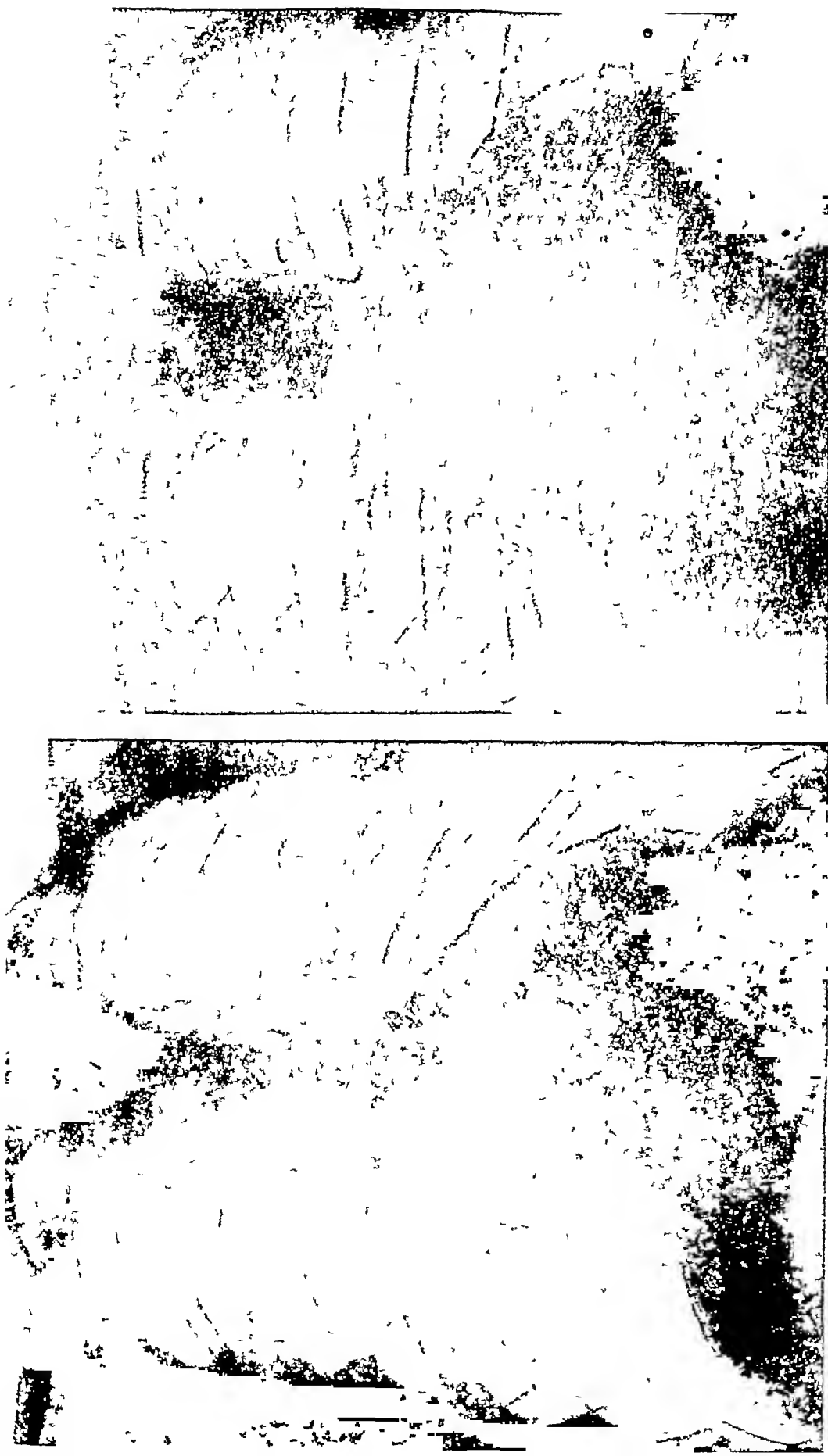
Fig. 5   Teleradiograms of enlarged hearts

A

B
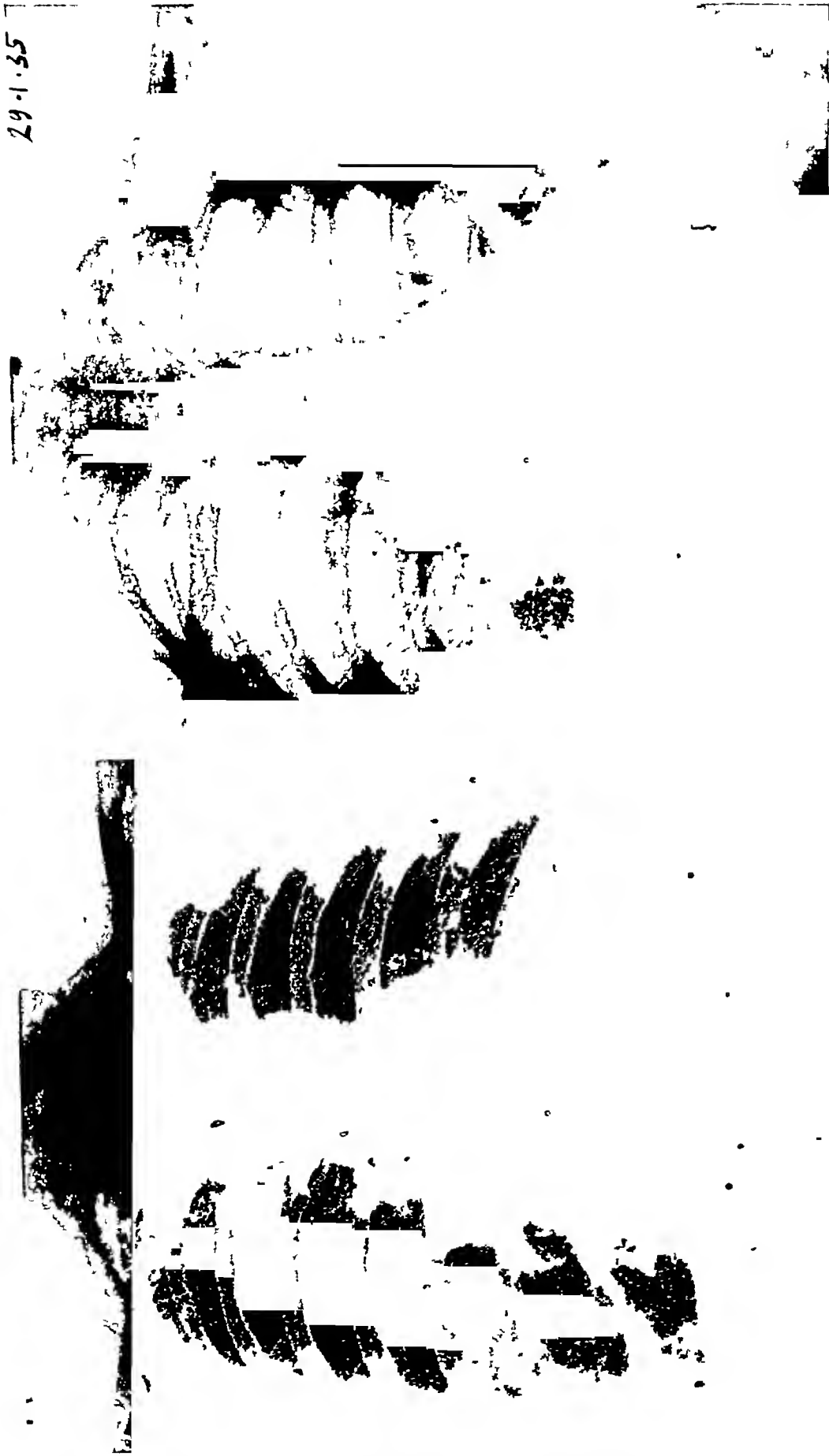
Fig. 6.—Teleradiograms from two women with enlarged hearts. Both show a shadow in the angle between the aorta and the right clavicle, possibly an abnormal origin of the right subclavian artery. (A) Case 3, aged 37, during her third pregnancy. There was no significant change in the size of the heart in 15 years from the age of 25 to 40 years in spite of a blood pressure of 230/120. (B) Case 4, aged 17. Pulsation in the neck was unusually striking. There was free aortic regurgitation with a B.P. of 200/90. On the right the root shadows are increased more than usual and there is a triangular shadow under the clavicle on the left the border of the aorta is unusually straight. There is a suspicion of notching on the second right rib. The patient died 11 months later probably of pneumonia but there was no necropsy.
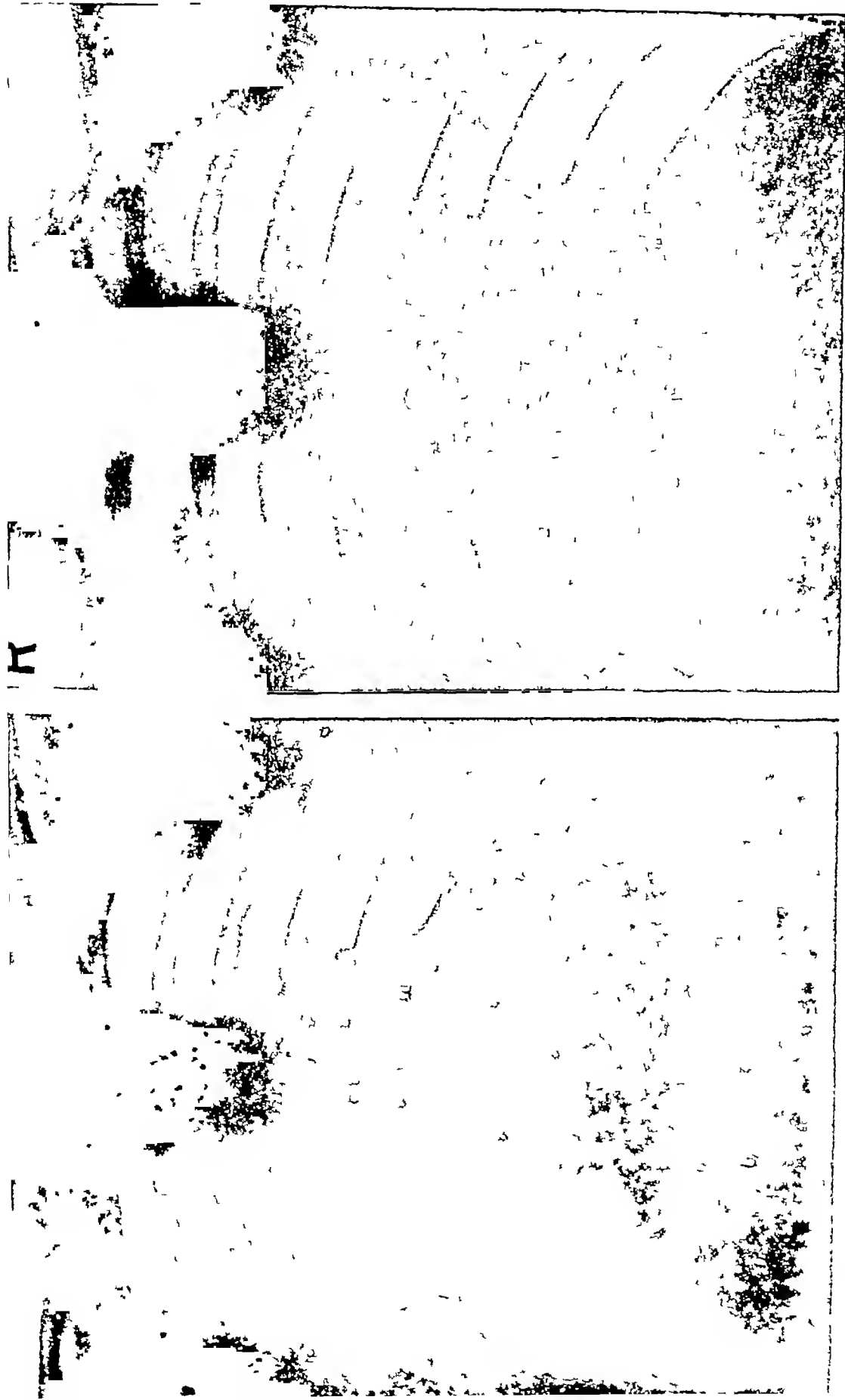
Fig. 7.—Teleradiogram to contrast large and small hearts   (A) Case 11 aged 27 with large rounded left ventricle a faint aortic diastolic murmur, and a B P of 195 100
(B) Case 14 aged 19 with a rather small centrally-placed heart, and a B P of 165 105

B

A
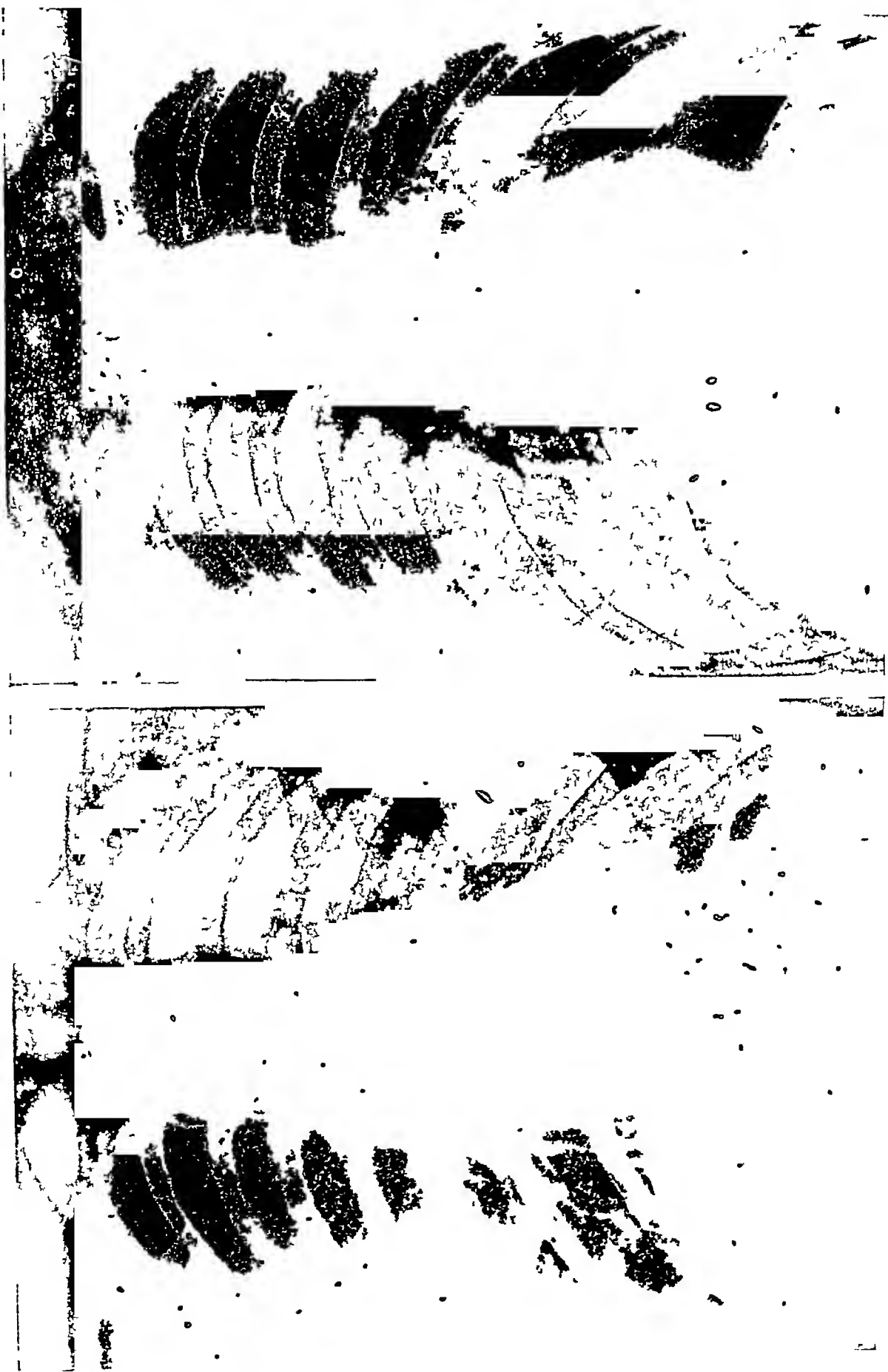
FIG 8 —Teleradiograms from Case 5 after an interval of 10 years   In each case the heart was of normal size without evident enlargement of the left ventricle   There is a curved shadow on the right at the level of the aortic arch, and the double curve on the left is well seen   (A) Case 5, aged 19   (B) Case 5, aged 29   The cardio-thoracic ratio is unchanged—10 5/24 5 in 1937, and 11 2/26 in 1947, both being 0 43   This is an example of the least increase in rib-notching over the 10 years

Case 6, aged 13   Although the blood pressure was already high and did not increase further, rib notching was only slight when he was first seen, the sixth left rib showing suggestive notching   Ten years later, when he was seen again, there were many areas in several ribs on both sides showing obvious shallow notchings (see Fig 5A)

Dr W St C Symmers has given us details of a case he saw where the notching of the ribs was not present in a routine X-ray taken when he was 16 (1929) but was obvious when he was 30 years of age (1943)   He had no symptoms, but at a routine examination in the Navy he had forcible pulsation in the arteries of the neck, some enlargement of the heart, systolic and diastolic murmurs widely conducted from the base, and a blood pressure of 195/95 (right arm), 185/95 (left arm), and 105/75 in the leg   No pulse could be detected in either femoral artery   The X-ray of 14 years before was obtained and no notching or enlargement of the heart could be seen   In 1940 he had been examined by the Naval Mass Radiography Unit without comment, and the radiologist who re-examined it in the light of the subsequent findings said that it showed no abnormality

Thus in all the cases followed for some years from childhood or early adult life, there was an increase in the depth of the notching or in the number of ribs affected or in both, though no doubt a stage is reached—later than the stabilization of blood pressure or even the development of the collateral circulation—when there is no further increase in the erosion of the ribs

There seemed to be no correlation with the blood pressure, the murmurs, or the size of the heart, and only a limited correlation with the extent of the superficial collateral circulation, the notching of the ribs continuing to increase to a later age   Other points, especially the site and distribution of the notches and the mechanism of their production have been dealt with by Bramwell and Jones (1941)   they state that it does not occur on the second rib but we think we have seen it there once, perhaps due to an abnormal artery (see Fig 6)

THE SIZE OF THE HEART

Lewis (1933) pointed out that there might be no progressive enlargement of the heart over many years and stated   " Cases do occur and are not infrequent in which with very high blood pressure the heart presents no sign of enlargement clinically even when examined by means of X-rays   It is improbable, however, that increased weight of the heart can be excluded by these means "   And, in fact, Peacock (1860) found the heart generally enlarged in 18 of 40 cases, while in 10 others there was a moderate increase affecting chiefly the left ventricle, and Abbott (1928) found some enlargement in 154 of 200 cases where there was necropsy evidence

It is clear, however, that high blood pressure in coarctation of the aorta does not produce as much enlargement as might be expected   Judged by the cardio-thoracic ratio many cases would be said to have no enlargement, but some degree of hypertrophy of the left-ventricle seems usual though not constant as judged by the rounded contour of the left border of the heart (see Fig 4, 5, and 7)   Where there is much enlargement additional causes should be suspected, such as associated congenital defects, the development of aortic regurgitation often on the top of congenital bicuspid aortic valves, or secondary changes in the heart muscle, which in the cases of pure high blood pressure without the associated factors of ordinary hypertension may be delayed for very many years

Of our 15 cases, 8 showed no enlargement or only a little enlargement of the left ventricle, as shown by some rounding of the left border, and 7 showed this in a more developed form so that there was some general increase   The maximum transverse diameter and the size of the chest for all our cases are given in Tables I and II

Of the 7 with enlarged hearts, 4 had an aortic diastolic murmur (Cases 1, 4, 6, and 11) so that no doubt this was partly responsible for the increase in size   In the remaining 3 (Cases 3, 7 and 13) aged 25 to 36 years the blood pressure averaged 215/112 (230/120, 250/120,

Q

and 165/92 respectively) In the four with diastolic murmurs the readings were 155/68, 200/90, 205/85, and 195/100 respectively (average 189/86, or 200/92 excluding the child)

There are considerable differences in the shape of the heart in coarctation, the only common feature being the left ventricular enlargement present in many cases The differences in the shadow of the aortic pedicle are even greater and for this reason we have reproduced several films to illustrate different types

The absence of the aortic knuckle in the radiogram has been emphasized as another classical sign of coarctation This with a straight left border is well shown in Fig 3A, 5B, and 6B In other cases, as Bramwell (1947) has pointed out, there is a striking double curve the upper generally representing the tortuous and dilated subclavian artery and the lower the blind end of the descending aorta (see Fig 7A and 8) In the paper by Hamilton and Abbott (1928) there are on successive pages a radiogram and a photograph of the specimen post-mortem and the correspondence of the upper curve with the subclavian artery is well shown Fig 5A is unusual in looking more like a case of aortic incompetence (which it was) with an apparent aortic knuckle

In some cases there are unusual shadows on the right, in the angle of the clavicle and aorta, possibly an abnormal right subclavian artery (Fig 6), and lower down on the right (Fig 4A) The root shadows are often prominent and were specially so in Fig 4C, 6B, and 7B

Two men with enlargement of the heart, especially to the left, are shown in Fig 5, and two women in Fig 6, in each case one had and one had not got aortic regurgitation possibly the shape of the aorta in Fig 5A is suggestive of aortic regurgitation, but this is not true of Fig 6B and otherwise the distinction could not be made on the X-ray film In Fig 7 another of the larger hearts is contrasted with a smaller one, both from young men of similar size and build

Of the 8 with little or no enlargement, 4 showed no enlargement clinically or radiologically (Cases 5, 9, 14, and 15, see Fig 7 and 8) The other 4 showed some rounding of the left ventricle only (Cases 2, 8, and 10, see Fig 4) or slight enlargement clinically without an X-ray being available (Case 12)

The other 6 with no general enlargement were between 18 and 33 years of age and the blood pressure readings gave an average of 190/108 which is not much below the average figure (215/112) for the three with moderate enlargement of the heart without an aortic diastolic murmur

It is clear from these figures that in some cases, but not in all, the enlargement of the heart can be correlated to some extent with the presence of a diastolic murmur, but not, at any rate at all closely, with the level of the blood pressure, as this may be just as high in those with no enlargement

Another point of interest is whether there is any progressive enlargement when the patients are followed for several years In the younger patients because of the natural growth of the chest as a whole, absolute measurements are not enough and the cardio-thoracic ratio combined with inspection of the contour of the heart is probably the best guide

In Case 1 the heart did increase in size over 6 years without much development of his chest, but he had aortic incompetence and an attack of rheumatic pericarditis (Fig 3) In Cases 2 and 5 (Fig 4 and 8) there was no progressive increase over 14 and 10 years

The first (Case 2) in spite of a rising blood pressure (to 210/105) and the development of an aortic diastolic murmur still had a cardio-thoracic ratio well under 0 5, though there seemed a little rounding of the left ventricle At 7 years the heart size was 9/19 cm with a blood pressure of 147/85 at 21 years it was 12 5/29 cm with a blood pressure of 210/105, so that the general growth of the chest was greater than the increase in the size of the heart (see Fig 4) In the second (Case 5) there was not even a suspicion of rounding of the left ventricle and the

cardio-thoracic ratio was 0 43 (10 6/24 5 when he was 19 and 11 2/26 when he was 29), although the blood pressure had remained over 180/110 during these ten years (see Fig 8)

In Case 3 there was possibly a slight increase during the period from 25 to 39 years of age but it was hardly significant   In the last (Case 6) followed from 13 to 22 years of age it seemed that there was a slight relative increase from (0 52 to 0 56) and that the heart was undergoing slight enlargement as well as natural growth

On the whole there is no progressive increase in the size of the heart with the high blood pressures of coarctation unless complicating factors arise   No doubt a balance is reached with some increase in the left ventricle, and even this may be absent

The relative absence of much enlargement is of theoretical interest also, because it is not found so often with other types of high blood pressure, presumably because in these cases the heart is also affected by the associated arterial disease, while in coarctation there is normal heart muscle to deal with the extra work   Graybiel, Allen, and White (1933) found no sclerosis of the arterioles or smallest arteries such as characterizes essential hypertension, and this probably applies to the coronary arteries also   These facts support the view that the importance of high blood pressure (and of valvular disease) in producing cardiac hypertrophy has been exaggerated   the size of the heart is also greatly influenced by whether the muscle is healthy or not and this helps to explain why the size of the heart is in most conditions of such great value in prognosis

Heart Murmurs

The Systolic Murmur   Characteristically, this is loudest to the left of the sternum in the second and third intercostal spaces   It may or may not be widely transmitted, but is nearly always heard in the back towards the left side, a point that was recognized early (Fawcett, 1905)   Sometimes there is a systolic thrill   In small children this systolic murmur may be the only physical sign noted and then other evidence of coarctation, especially the poor femoral pulse, should be searched for   When the collateral circulation is well-developed systolic murmurs may be heard very widely, but some of these may be produced in the tortuous and dilated arteries

A systolic murmur was noted in all these patients when they were first seen, but the two youngest were already 7 and the next youngest was 13 years   In one (Case 13) the systolic murmur was rather faint and insignificant and in two others it became so—in one naturally (Case 5) and in one after operation (Case 10)

Diastolic Murmurs   A diastolic murmur was heard at the base of the heart in 6 of our 15 patients   in one (Case 1) it may have been due to rheumatic aortic incompetence and in another (Case 2) without any obvious signs of infection it developed and gradually became more obvious, but without any fall in the diastolic pressure when he was between 10 and 14, in the other four it was noted when they were first seen at 13, 17, 17, and 25 years of age respectively, and the readings of the blood pressure were 210/80, 200/90, 195/100, and 170/105 (average 194/94)   Perlman (1944) reported it in 9 of 13 cases but this seems a higher proportion than usually

A high diastolic pressure is the rule in coarctation, even in most cases when there is an aortic diastolic murmur   It is only when there is a greater degree of aortic incompetence caused by superadded changes in the valves that the diastolic pressure is low   these may be rheumatic or other inflammatory or atheromatous changes   Thus in Case 1, with rheumatic aortic incompetence the diastolic pressure was at first 60 and later 45 mm   If the diastolic pressure is low infection of congenital bicuspid valves may often be suspected   Usually the diastolic pressure is relatively high even when there is a diastolic murmur   This probably means a slighter leak from atheromatous changes in bicuspid valves or perhaps even from some stretching of the aortic ring and it will be interesting to see if any of these diastolic murmurs disappear with surgical correction of the coarctation

THE ELECTROCARDIOGRAM

Lewis (1933) stated that there was generally left-sided preponderance 6 of his 8 cases showed it but 5 of them were over 40 and the 2 who did not were younger—24 and 37 years of age Brown (1939) considers there are no characteristic changes and that normal axis deviation is often present though left axis deviation generally develops

Of our 13 patients with cardiograms Case 1 developed left from some right axis deviation in the six years of observation, but as this and the increase in size of his heart may have been the effect of his increasing rheumatic aortic incompetence it is hardly fair to include him Only 3 of the other 12 had left axis deviation—Cases 3 (25–37), Case 4 (17), and Case 7 (36)—the figures in brackets giving the ages at the time they were under observation One, Case 2 (7–20), had well-marked right axis deviation The remaining 8 had no axis deviation but it is of course possible they may develop it as they are all under 33 years of age

It is, however, obvious from these figures that the electrocardiogram is of no value for diagnosis, as normal is more common than left axis deviation The rounded left ventricle in radioscopy gives a better indication of the extra work put on the left ventricle, even when there is not enough enlargement to make the total measurements outside the normal range The cardiogram is, of course, of interest and may be helpful in deciding on the presence of other abnormalities

Other changes in our cases were T I, T II, and T III inversion (Cases 6 and 7), T 1 inversion (Cases 1 and 4), a biphasic T I (Case 14), slight widening and notching of QRS (Cases 2 and 15), Q III (Cases 12 and 13), an inverted P III (Cases 7 and 10), a biphasic P III (Case 14), and a prolonged P–R of 0 19 sec (Case 10), of 0 20 sec (Case 14), and of 0 22 sec (Case 12)

THE BLOOD PRESSURE

All writers agree that, with rare exceptions, the blood pressure in the upper part of the body is raised Lewis (1933) found high blood pressure present in all his adult cases, and that in general it had no further tendency to rise and only fell terminally or with congestive failure Often the symptoms seem very slight compared with what might be expected for the degree of hypertension, even where the rise of pressure is known to have been present for years Our findings are given in Tables I and II In general we have found the pressure rather variable from visit to visit and we, therefore, attach more significance to average figures, some representing a large number of readings taken over a period Reifenstein et al (1947) have also commented on the variability and quote a case where reading of 122/80 and 180/85 were recorded King (1937) quotes some similar cases—238/128 to 178/90 (Flexner), 210/170 to 160/90 eighteen months later (Lichtenberg et al)—but such cases are, of course, quite exceptional We think the difficulty of measuring the blood pressure in the legs has not been stressed sufficiently We have found no constancy as to whether it is easier by auscultation over the popliteal or by palpation of the posterior tibial or dorsalis pedis, we have often failed to get a convincing reading, though perhaps later in the same patient it has not been difficult to get a decisive level

The average figure in our patients was 203/105 in the right arm, though in many we obtained one or more readings about 20 mm higher than this, and 130/85 in the leg, there were some where we could get no convincing reading of the diastolic pressure in the leg These figures are very close to those of Lewis (1933)—207/105 in the arm and 116/— in the leg

Rarely the pressure is much lower in the left arm because the left subclavian has its origin below the coarctation (Bayley and Holoubek, 1940) We have not encountered an example of this but have found three cases where many readings gave a persistent difference presumably due to tortuosity of the arteries or unnatural angles of flow of the blood stream Reifenstein et al (1947) attribute this difference which was present in many of the cases collected by King (1937) to pressure of the distorted aorta above the coarctation on the left subclavian

In our Case 3 the figures were 235/118 in the right arm and 220/112 in the left, in Case 13, 165/92 in the right, and 155/92 in the left, and in Case 5, 180/107 in the right and 167/102 in the left, and ten years later 186/120 and 175/110 respectively All these figures were the average of a large number of readings often by various observers

TABLE I

BLOOD PRESSURE AND SIZE OF THE HEART IN CASES OF COARCTATION OBSERVED OVER SOME YEARS

Case No and Sex	Age (in years)	Blood Pressure		Size of Heart		
		Rt arm	Leg	m t d (cm)	Chest (cm)	C–T ratio
1* Male	7	142/70	100/50	11 5	21	54
	10	155/70	95/60	13 5	21	64
	12	157/72	—	(17 0	21 5)†	—
	13	165/60	110/—	15 0	22	68
2 Male	7	147/85		9 2	19	48
	9	159/88		10 0	20	50
	11	176/95	110/60	10 0	21	48
	14	180/100		11 0	24	46
	16	210/110		—	—	—
	21*	210/110	125/—	12 5	29	43
3 Female	25	230/120		14 0	—	—
	28	210/110		13 5	25	54
	38	230/120	120/85	15 5‡	27 5‡	56
	40	240/120		14 5	25 5	57
5 Male	19	180/107		10 5	24 5	43
	29	185/120	115/—	11 2	26 0	43
6* Male	13	210/80	115/90	13 0	25	52
	22	200/85	125/—	15 7	28	56

* With an aortic diastolic murmur
† During rheumatic pericarditis
‡ During pregnancy

TABLE II

BLOOD PRESSURE AND SIZE OF THE HEART IN COARCTATION OF THE AORTA

Case No	Sex and Age	Blood Pressure		Size of Heart		
		Rt arm	Leg	m t d (cm)	chest (cm)	C–T ratio
4*	f 17	200 90	140/90	14 5	26	56
7	m 36	250/120	160/120	15 0	28	53
8	m 30	190/—	120/—	—	—	—
9	m 29	230/130	135/? 85	13 0	28	46
10	m 30	190 110	120/80	12 5	28	45
11*	m 27	195 100	130/90	14 0	27	52
12	m 33	195 90	140/—	—	—	—
13	m 27	165 92	130 —	16 3	31	52
14	m 18	165 105	—	11 0	27 5	40
15*	m 26	169/107	110 90	13 5	29	47

* With an aortic diastolic murmur

THE RISE IN BLOOD PRESSURE

Cases of coarctation are rarely diagnosed clinically in infancy, and this is partly because the pressure does not rise greatly for some years

Lewis (1933) wrote "It may seem natural to assume that if high pressure is found in the adult case, it has been present from the first year of life, but experience shows that such assumptions are not without danger the conclusion that coarctation represents life-long high pressure becomes more and more justified as these pressures are recorded over longer periods In this series there are records of high pressure extending over 5, 6, 6, 9, 13, 15, and 16 years We still lack records covering childhood and adolescence"

Lewis (1933) collected the records of some reported cases with readings of the blood pressure, but only four of these were under 20 years Since then Hunter (1928) has reported a boy of 14 with a pressure of 165/90, Hampson (1931) one of 12 with a pressure of 145/75, and Moncrieff (1931) a child of 6 with a pressure of 150/100 Wilkinson (1932) reported a child aged 4 with a pressure of 150/80 in the arms, a feeble iliac pulse, but no obvious collateral circulation, another, aged 14, with a pressure of 198/135 in the arms, no palpable pulse in the leg, and a well-developed collateral circulation, Sheldon (1932) one, aged 12, with a pressure of 150/100, no palpable femoral pulse, and some collateral circulation, and Rooke (1938) a boy, aged 3, with an arm pressure of 150/85, an absent femoral pulse, and a fairly well-developed collateral circulation but no visible notching of the ribs

King (1937) made a very complete collection of all the reported cases with readings of the blood pressure and Steele (1941) continued this, both including some additional young cases

We have found few records of the development of this high pressure, but in Case 2 of Farris (1935) it was 120/80 when he was 9, 142/70 when he was 15, 160/90 at 17, and 166–180/74–90 at 19 years Schwartz and Tice (1939) describe a boy where it was said to be "normal" at 15, 180 at 18 when examined for life insurance, and 176/107 at 23 years Steele (1941) reports a case where it was said to be "raised" at 10, and was 220/110 at 33 years

Two of our cases illustrate this rise of pressure, one especially well as it was observed rising from 7 to 16 years of age when it began to stabilize, in a third case the maximum had certainly been reached by 13 and no change took place in the next 10 years Of course the variation may be wider than this though we think it unlikely that there is any further rise of pressure after the period of growth is completed

The two youngest cases in our series were 7 years old when the diagnosis was first made In both these the pressure gradually increased In Case 1 it averaged 142/70 in 1932–3, 155/70 in 1935–6, 157/72 in 1937, and 165/60 in 1938 when he was 13 and was lost sight of the low diastolic was no doubt due to aortic incompetence

Case 2 was seen originally because of the blood pressure after scarlet fever, though investigations showed no renal changes In 1933, when he was 7, the pressure averaged 147/85, in 1934–6 it averaged 159/88, in 1937, 176/95, and in 1938, 165/100, in 1940 a single reading was 180/100, in 1942, 210/110, and 1946, when he was 20, 210/105 In this case the pressure rose from 147/85 when he was 7 to 210/110 when he was 16, and then began to stabilize

None of the other cases were as young as these two when they first came under observation and the pressure already seemed to have risen to a level that has been maintained without much change In Case 6 the blood pressure was already 210/80 when he was 13 and is 200/85 nine years later, in Case 4 it was 210/87 when she was 17 years old (she died later that year), and in Case 5 it was from 200/120 to 180/107 when he was 19 and 185/120 ten years later

In the older patients we only have one with a long series of blood-pressure readings over many years, in her it showed no significant change from 25 to 40 years of age, being about 230/120 when she was up and about and 190/100 to 205/110 when she had been resting

These three cases with no great change in the pressure during ten years agree with Lewis's view that the blood pressure can remain at a steady high level for a great number of years till death or the onset of congestive failure His cases were older than ours, the two youngest being 20 and 24

Apart from these individual patients followed over some years we have approached the problem in another way   We have taken the average figure for the blood pressure for each age from all the cases mentioned here, from all tabulated by Lewis (1933), by King (1937), and by Steele (1941), and from our own cases   Where these have been followed for some years with frequent readings of the blood pressure they have been included once for each year of observation and a few other reported cases have been included more than once where the data were available

With the relatively small numbers available (85 values between 3 and 19) and the great variation the average figures for each year are very erratic but there seems no doubt of their becoming gradually higher   To make the numbers in each group a little larger all cases up to 7 were combined, those aged 8 or 9, those aged 10 or 11, etc, and from these averages Fig 9 has been constructed   It appears that there is a steady rise from 5 years to 16 or 18 years after which the rate of increase tends to be less steep   We have found no adequate data below the age of 5 years
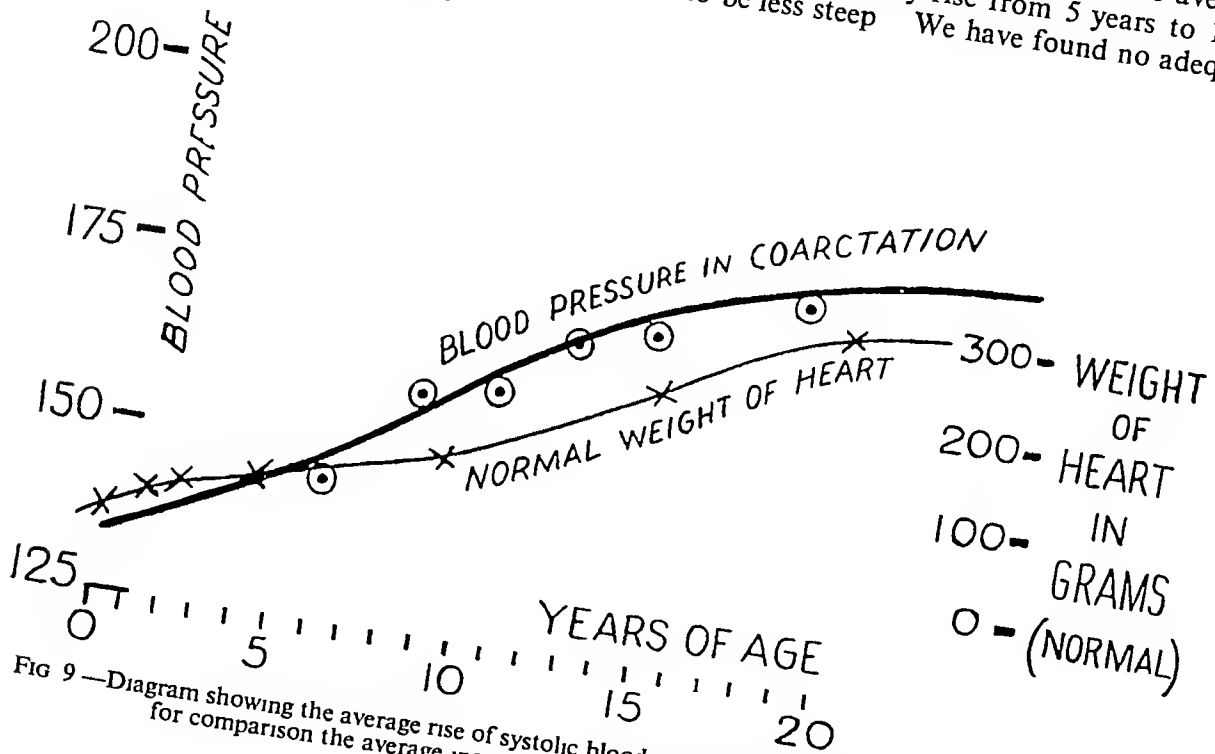
FIG 9 —Diagram showing the average rise of systolic blood pressure with age in coarctation (see text) and for comparison the average increase of weight of the heart in normal children

This fits in with the view that the blood pressure rises most quickly during the period of most rapid growth   The increase in the weight of the heart with age has been plotted on the same diagram from the figures given by White (1931)   This probably gives a nearer approach to the increase in size of the aorta than the increase of body weight as a whole would, partly because of their closer functional relationship and partly because the heart increases less with age than does the body weight, the heart being 1/130th of the body weight at birth and 1/200th of the body weight in adult life (Quain's *Anatomy*, Vol II, Part 2, p 374)

There is some general resemblance between the shape of these two curves, one for the rise of the blood pressure in coarctation and the other for the normal increase in the weight of the heart, and this supports the view that the rise of blood pressure during the period of most rapid growth is because the pathological stenosis of the aorta remains the same size, or does not increase at the same rate as the rest of the aorta   The consequence is that the obstruction

to the circulation becomes greater with a resultant rise of blood pressure and a resultant increase in the collateral circulation

Lewis (1933) suggested that it had not yet been proved that obstruction was the cause of the raised blood pressure and that such measurements as were available showed that the total area of the main arteries carrying the collateral circulation was much the same as the area of the aorta before the obstruction   If this is true it might be that in a slowly moving stream there would be no rise of pressure   In the arteries, however, the blood is moving with great speed and the pressure depends not only on the total calibre of the vessels but also on the resistance caused by contact with the vessel walls, and the more the main channel is divided into separate arteries and the longer the path, the greater will be the resistance from this point of view

It seems natural to assume that the high blood pressure proximal to the obstruction is the result of this obstruction   Nevertheless, several writers have suggested since Goldblatt's work on renal hypertension, that this factor is also at work in coarctation   But if such a humoral mechanism were at work it should affect the legs as much as the arms, and the fact that it does not do so or does not do so to the same extent, brings one back to the obstruction as preventing the transmission of the high pressure from above it to the area below it   In so far as there is a tendency for the diastolic pressure in the legs to be high such a humoral mechanism might be responsible, but it seems more naturally related to the small pulse pressure in the legs   This is to be expected from the slow steady flow that takes place into the legs through longer and more devious channels and tends to damp down the usual pulse pressure

Finally if operative removal of the obstruction is followed by a return of the blood pressure to normal as seems likely from the early reports (Crafoord and Nylin, 1945) this will support the view that the obstruction is the direct cause of the rise

PROGNOSIS

The possibility of surgical treatment of coarctation of the aorta has emphasized the need for a reasonably accurate prognosis   Fortunately there is evidence on which this can be based—more than we have in the case of patent ductus arteriosus, the relative lack of which have been pointed out by Gilchrist (1945)

The classic paper of Maud Abbott (1928) summarized what was known of 200 collected cases, all supported by the evidence of an autopsy   Of these, 70 per cent died between the ages of 10 and 40, and the deaths were almost equally distributed in these three decades. the mode being between 20 and 30 and the average age at death being just over 30 years

The causes of death were cardiovascular in four-fifths and from other causes in one-fifth in more detail, heart failure in 30 per cent, sudden cardiac deaths in under 10 per cent, ruptured aorta and related causes in 20 per cent, endarteritis in 7 per cent, and cerebral hæmorrhage, often from proved congenital aneurysms, in 13 per cent, these making 80 per cent of the total

Special reported cases might not give a fair impression of the ordinary prognosis but there are two series detailing all those dying in hospital during a long period from 1826 to 1902 in Guy's Hospital (Fawcett, 1905) and from 1909 to 1932 in the London Hospital (Evans, 1933) They not only agree in placing the total incidence at about one case of coarctation in each 1000 necropsies, but also in the average age at death which was 31 in Fawcett's series and 29 years in Evans's series, excluding those of the " infantile " type with multiple congenital defects who died in the first few years of life

Even these figures, being deaths in hospital, may be considered too pessimistic and it is, therefore, worth considering Bramwell's figures   The average age of his 10 patients who had died was 32, but this figure will be considerably increased as the average age of the 13 patients who were alive was already 35 years   The age of death in Lewis's cases (1933, and Bramwell, 1947, Table X) were older, just over 50, but these were patients who had been fit enough to serve in the army during the war of 1914–18   Bramwell concludes ' that patients whose

symptoms date from childhood are unlikely to reach the age of 30, whereas in those who are free from symptoms until the age of 30, the further expectation of life is much more favourable ''

As these older patients, free from symptoms up to 30, are less likely to be thought suitable for operation, the other figures are all in rather close agreement that the prognosis of those with symptoms cannot be described as better than fair, with an expectation that on the average life is not likely to be prolonged much beyond 30 years

It seems, therefore, that successful operative treatment has much to offer, provided the risk is not too great and that the fall of blood pressure found in the early cases proves to be general, as seems likely on theoretical grounds   But the risk of a fatal accident from other congenital abnormalities should not be forgotten, especially from rupture of a cerebral aneurysm, though the fall in blood pressure may help in preventing this catastrophe

SUMMARY AND CONCLUSIONS

Coarctation of the aorta still passes unrecognized   It will continue to be missed if a striking collateral circulation is always expected to be self-evident   It will be diagnosed if the femoral pulse is felt for and the blood pressure taken in the legs in every case with high blood pressure or with basal systolic or diastolic murmurs, or with undue pulsation in the neck, when these are without an obvious cause

The collateral circulation can be demonstrated in many patients when it is not evident, or made more obvious in others, if the patient is made to stoop forward with his arms hanging down vertically while his back is examined in a good light   This is because the greatly dilated subclavian artery is compressed between the clavicle and the first rib   bending forward opens up the costoclavicular space and so releases this pressure on the subclavian artery   Any movement that increases the costoclavicular space may demonstrate this sign

A high pressure in the arms with a low pressure and a poor femoral pulse, or the demonstration of a collateral circulation are pathognomonic of coarctation of the aorta   They are even more important than notching of the ribs, not only because X-rays are not always available, but because they are present at an earlier age

The rise of blood pressure, the collateral circulation, and the notching of the ribs develop as a rule between the ages of 6 and 16, but more information is needed about cases at the younger ages   The blood pressure seems to stabilize first, at about 14 to 18, the collateral circulation continues to develop rather longer, and the notching of the ribs still longer

The rise of blood pressure and the increase in the collateral circulation occur during this period of rapid growth, we suggest, because the stenosis of the aorta does not increase in cross-section (or increases relatively little) with the growth of the rest of the aorta so that the relative obstruction becomes greater

Average figures for the blood pressure are about 200/105 in the arm and 130/85 in the leg   Thus in the arm there is a greater rise of the systolic than of the diastolic blood pressure   In many cases with an aortic diastolic murmur the diastolic pressure remains fairly high   The relatively normal diastolic reading in the legs is against the view that there is a genuine hypertension following renal ischæmia

More than half our cases had little or no clinical or radiological enlargement of the heart, though this cannot exclude some small increase of weight and the left ventricle was often rounded   Enlargement was more likely where there was an aortic diastolic murmur (6 of 15 cases) though even then it was sometimes slight   As Lewis found, the heart may not increase in size during many years' observation

The electrocardiogram is of no value for diagnosis   left axis deviation was present in only a quarter of these patients, aged 7 to 39 years

The average expectation of life of those with symptoms before adult life is probably no

more than 30 years, so that cure by operation has something to offer   Where the diagnosis is made for the first time in adult life, and especially in those without symptoms, the outlook is relatively good

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APPENDIX OF CASE NOTES

Case 1, aged 7 (1932)   This boy had whooping-cough and measles and several attacks of bronchitis, and his first school medical examination without comment on his heart   When he was 6, his doctor recorded an aortic systolic murmur   When 7 he was n the Brook Hospital and Dr Young noted that his murmur had not changed during his attack of scarlet fever and sent him to outpatients with the suggestion that he might have coarctation

He was found to have a rough aortic systolic murmur and thrill and a soft aortic diastolic murmur both best heard to the left of the mid-line   A systolic murmur could be heard at the apex also and the diastolic was more rumbling   The blood pressure in the arms varied between 140–160 systolic and 55–85 diastolic, the latter being somewhat difficult to determine at times   In the legs it was 100/50 and the femoral pulses were hard to feel

There was visible arterial pulsation round the scapulæ and shoulders and rib-notching on X-ray, though this was faint (see Fig 3)   The left ventricle seemed slightly hypertrophied (*see* Table I) and the aortic knuckle was not prominent   The diagnosis of coarctation of the aorta seemed conclusive, though there was some doubt whether he had in addition rheumatic valvular disease (A S and A I , and possibly M S) or perhaps regurgitation from bicuspid aortic valves with some added stenosis

During that winter he had some attacks of bronchitis at home, and when seen in March 1933, had a small right-sided pleural effusion   He made a rapid recovery in hospital and the fluid disappeared in three weeks   The general physical signs were unchanged   the collateral circulation seemed more obvious though pulsation in the femorals and abdominal aorta was still noted

During the next three years he kept well, but in July 1936, when 11 years old, was readmitted with rheumatic pains, loss of weight, and increasing dyspnœa   Comparing his condition with four years before, the systolic blood pressure and the size of the heart relative to the chest seemed to have increased a little (see Table I)   The rib-notching and the collateral circulation were more obvious

His illness need not be detailed, but after ten days the temperature rose to 104° and continued about 101° F for five weeks   Rheumatic carditis and infective endocarditis were considered and the former was confirmed by the occurrence of rheumatic nodules and the development of pericarditis with effusion, the transverse diameter of the heart shadow increasing from 14 0 to 17·0 cm (see Fig 3)   He made a gradual recovery, but from this time onwards he was more breathless and complained of pains in the legs and bronchitis from time to time

He was last examined in 1938 when he was 13   The apex beat was more heaving and the diastolic murmur was a little louder, both at the base and in the mitral area   The systolic pressure and the size of the heart had again increased a little (see Table I), the pressure in the arms being 165/60 and in the legs 110/?   The rib-notching was slightly deeper and more clear-cut

In this boy as he grew from 7 to 13 years of age the heart increased in size from 11 5 to 15 cm with very little increase in the size of his chest or general development   His murmur also increased, but this and some of the increase in the size of his heart may have been due to the complication of his rheumatic carditis   The blood pressure, however, rose from 142/70 to 165/60 (probably with a greater degree of aortic regurgitation) and the signs of the collateral circulation increased, though the rib-notching did not increase so much as in some

Case 2, aged 7 (1933)   This boy was seen because he did not seem to have regained his normal health after two attacks of pneumonia the year before   There was a rough systolic murmur at the base and the blood pressure was 140/90   He was taken into hospital to exclude infective endocarditis or nephritis   There was, however, no pyrexia and the urine was normal

One of us (S S) already wished to diagnose coarctation of the aorta on a poor femoral pulse, some visible arterial pulsation round the scapula, and a suspicion of rib-notching (see Fig 4)   These signs were at this stage so slight that the other was not convinced and wrote that the only certain findings were an average blood pressure of 147/85 and a little enlargement of the left ventricle   A year later, however, this diagnosis was made with certainty as the average pressure was now 159/88 (170/95–150/80) and the collateral circulation was more easily seen

By 1936, when he was 10, there had been no further increase in the blood pressure or in the size of the heart   His general condition was improved though he was a little breathless if he tried to keep up with the other boys at school

He was seen frequently during 1937 and many readings of the blood pressure were taken with an average figure of 176/95   The collateral circulation was now more easily visible and palpable   the femoral pulse was very difficult to feel and the pressure in the legs was recorded as 110/60, he had sometimes complained of aching in the legs   Rib-notching was more easily seen on X-ray (see Fig 4) The basal systolic murmur was rather louder when he was lying than sitting and sometimes a systolic thrill could be felt

He had been rather undersized but during 1937–9 and the first two years of the war when he was away in Devonshire he grew a good deal and developed generally   The blood pressure still continued to rise to 165/100 in 1939, to 180/100 in 1940, and to 210/110 in 1942   The size of the heart had increased from 10 cm in 1937 to 11 cm in 1940

By 1946, when he was 20, the signs of coarctation were typical and well-developed though he considered himself in good health and was working as a bank clerk   It was difficult to feel any pulsation in the femorals or abdominal aorta and the pressure in the arm seemed to have stabilized at 210/105 The collateral circulation was even more easily seen than four years before and was now visible over the front of the chest as well as along the lower costal margins   The rib-notching had increased and the arterial pulsation in the neck was now much more visible than when he was a boy   The murmurs had increased as well and systolic and diastolic murmurs could be heard both at the apex and at the base with a long systolic thrill at the base   Originally there had only been a rather faint systolic murmur at the base which had gradually increased in loudness and in its area of distribution The diastolic murmur had developed during 1936–40 (when he was from 10–14) and at first had seemed like a reduplicated second sound at the apex, so that taken alone this simulated the signs of mitral stenosis   The heart had also steadily increased in size from 9 cm at the age of 7 years, when there had seemed to be some ventricular enlargement only, to 11 cm in 1940, and to 12 5 cm in 1946, when there was a general increase in the size of the heart both to left and right, but the relative increase was not as much as the absolute increase, since the chest had also increased with his growth to a greater extent, i e from 19 5 to 29 cm   There were no further changes in 1947   He was one of the patients when bending down made the arteries in the back and side, previously only visible under the left scapula, much more obvious and widespread (see Fig 2)

Case 3, aged 25 (1932)   This woman had no complaints till after a stillbirth in her second pregnancy when she was 25   She was then a little short of breath, and was found to have slight enlargement of her heart to the left and a blood pressure of 230/120   She was advised to take some extra rest and to have no more children

Three years later she was seen again as she had become pregnant, and the correct diagnosis was made   The B P was 210/110, the heart was enlarged to the left (13 5 cm m t d in chest of 25 cm), and there was forcible pulsation in the neck, simulating aortic regurgitation, and a systolic murmur and thrill loudest at the base of the heart   A collateral circulation was demonstrated over the abdomen and round the scapulæ and there was notching of the ribs on X-ray examination   Her pregnancy continued normally and a living child was born at term

She left London and was lost sight of till 1944 during the fourth month of another pregnancy Her general condition had continued to be good, but the collateral circulation was now more striking than before and could not have been missed   The other physical signs were unchanged and the B P averaged 230/120 (the same as in 1933), falling to 190/100 when she had been in hospital some days The femoral pulse was difficult to feel and the B P in the legs was 120/85   The heart seemed rather larger, 15 5 cm m t d in a chest of 27 5 cm , but this was due to displacement owing to the pregnancy (see later and Fig 6)

The cardiogram showed left axis deviation and was otherwise normal though some records in 1936 had shown some inversion of T III

She was readmitted for her confinement in May 1945, aged 38, and the average of many blood pressure readings was 235/118 in the right arm and 220/112 in the left arm   Her renal function tests had been normal some months before, but as signs of toxæmia developed a healthy premature infant was delivered by Cæsarean section   Some urinary infection cleared up and she made a good recovery and was discharged home with a blood pressure averaging about 205/109

In 1947, when she was 40, she was in good health and doing most of her ordinary housework The B P at an outpatient visit was 240/120   The heart was very little larger than in 1935, only 14 5 cm

in a chest of 25 5 against 13 5 cm in a chest of 25 cm   The collateral circulation in the back became much more obvious on bending

In this case, in spite of a blood pressure of 230/120 when she was 25, the patient was in good health when 40, and able to go through a pregnancy when 38 years old   There had been no further rise in her blood pressure and only a slight further increase in the size of the heart

Case 4, aged 17 (1935)   This girl came to hospital because of a hoarse voice, which had been getting worse for some time, it had not been improved by tonsillectomy when she was 10   Pulsation in the neck was noted then and had got worse since she was 14, but she had no other symptoms and had played all games at school   Her heart had not been mentioned till she was 14, though she had been under observation because of her nose and throat for six years

Mr Mollison reported that the left vocal cord moved less well than the right   Her face looked bloated and she said that her face and lips often swelled up in the morning   There seemed a large pulsatile swelling low down in the neck on the right side   Because of this and the most unusual degree of pulsation on the right side of the neck it was thought at first that she might have an angioma acting like an arterio-venous aneurysm, but in view of the murmurs and other findings this was probably due to aortic incompetence and abnormal vessels from the right side of the arch (see Fig 6) with a considerable collateral circulation through the thyroid

She had systolic and diastolic murmurs loudest in the pulmonary area with a systolic thrill   The heart was enlarged to the left and the B P was 220/95 in the arm and 140/90 in the leg   No collateral circulation was seen as she was well-covered but it was easily felt   X-ray showed notching of the ribs, an absence of the aortic knuckle, and an extra shadow above the arch of the aorta below the right clavicle (? abnormal arterial branches)

The right pulse seemed stronger than the left and though the readings were variable they averaged 205/95 in the right and 190/90 in the left arm

She was seen several times between January and August and said she was well but perhaps a little more breathless   In December she was admitted to St Olave's Hospital and died in a few days   The diagnosis made was " aortic incompetence and pneumonia," but unfortunately there was no necropsy

Case 5, aged 19 (1937)   This boy had been able to do a good deal without dyspnoea, but for four months had noticed increasing fatigue, especially after gymnastics, and headaches   There was increased pulsation in the neck and the collateral circulation was easily seen   Rib notching was conspicuous

The blood pressure was sometimes as high as 200/130   The right pulse was felt more easily than the left and the average pressure was 180/107 in the right, and 167/102 in the left arm   The femoral pulse could not be felt   There was no enlargement of the heart (see Table I and Fig 8)   There was a loud systolic murmur at the base, faintly heard towards the apex, but no thrill

He was seen again in 1947, aged 29   He had passed into the R A F without comment, graded A1, and had served 6 years, mainly doing clerical work in the Middle East, but taking part in all physical exercises and keeping very fit   His heart condition was noted—for the first time in the R A F—and correctly diagnosed on demobilization   His only symptom was tiring too easily after exertion

The collateral circulation in the back was perhaps less easily seen than in 1937, but over the abdomen it was very striking   The notching of the ribs was a little deeper and more clear cut (see Fig 8)

As before the right pulse was more easily felt and the pressure was 200–175/120 in the right and 180–170/110 in the left arm   Pulsation could not be felt in the abdominal aorta and barely in the femorals and the blood pressure in the leg was 115/?

There was no enlargement of the heart and no change in its shape, the bulge in the region of the aortic knuckle being probably due to the enlarged subclavian artery   The systolic murmur at the base was still present, but was fainter and almost insignificant and was certainly much less than ten years before   The electrocardiogram showed no left ventricular preponderance, but slight widening of S in all leads   all T waves were upright though T III had been inverted in 1937   This was another case where bending down increased the collateral circulation and made it much more visible (Fig 2)

Case 6, aged 13 (1938)   This boy was sent to hospital because of the undue pulsation that had been noted in his neck   He admitted to some recent dyspnœa but said that till recently he had been able to play all games without difficulty

There was striking pulsation in the suprasternal notch and the blood pressure was about 210/80 in both arms and 115 in the legs with a poor femoral pulse   Some collateral circulation was found with difficulty but only over the back, there was slight rib notching

The heart was just enlarged, and there were loud systolic and diastolic murmurs at the base, so that he probably had aortic regurgitation as well as the coarctation

He was seen again in 1947, aged 22 years   He was well built and of normal height and had been passed into the Navy during the war without comment   After some months, however, a medical orderly had drawn the doctor's attention to the pulsation in the neck and he had been discharged from the service   He had since worked regularly as an engineer, but admitted to some breathlessness with heavier exertion

The physical signs were in general the same though there had been some increase   The pulse and blood pressure were the same in both arms falling from 230 to 195/85, it was difficult to feel any pulse in the abdominal aorta or femorals and the pressure was 125   The pulsation in the neck was perhaps even more striking, the collateral circulation was still seen and felt only after a careful search, but it could now be found along the sternal border as well   rib notching was moderate

The heart had increased in size to 15 7 cm in a chest of 28 cm and the enlargement was mainly of the left ventricle (Fig 5)   An apparent aortic knuckle was probably the subclavian artery   The systolic and diastolic murmur at the base of the heart seemed louder and could also be heard at the apex, the former murmur suggesting that perhaps the degree of regurgitation had increased from progressive atheromatous changes, though there was no increase in pulse pressure to confirm this   The aortic second sound seemed accentuated and there was a long systolic thrill at the base   There was also a diastolic shock on palpation in the aortic area

The cardiogram now showed T I inversion as well as the T II and T III inversion that had been present in 1937   As there was a large R III with no S III it was nearer right than left ventricular preponderance but was really of the R R R type   These findings with the aortic diastolic murmur left some doubt as to what lesion was present as well as the coarctation   in spite of the cardiograms aortic regurgitation seemed the most likely

Case 7, aged 36 (1940)   He was rejected for the Navy at 20 because of his heart   He continued with heavy work although he was a little short of breath   A year before he had been giddy and had become unconscious for an hour—an episode suggestive of a congenital cerebral aneurysm   He was a healthy well-developed man with a little enlargement of the heart to the left, and a fairly loud and widely conducted systolic murmur   There was forcible pulsation in the neck and a poor femoral pulse   The blood pressure was 260/120 in the arms and 160/120 in the legs   Arterial pulsation was clearly felt down the vertebral border of the scapulæ and wide shallow notches were seen in the posterior part of the 3rd to 7th ribs on the right side and the 4th to 9th ribs on the left side   We are indebted to Dr W Gover of St Leonards for details of this case   It has not been possible to trace him

Case 8, aged 30 (1942)   This officer was seen after pneumonia because of a harsh systolic murmur at the base of the heart   The femoral pulse was poor and the blood pressure was 190 in the arms and 120 in the legs   There was a collateral circulation round the scapulæ   X-ray showed no general enlargement of the heart, but, as usual, some rounding of the left ventricle, an absence of the aortic knuckle, and a moderate degree of rib-notching   He complained of no symptoms and has not been seen since

Case 9, aged 29 (1944)   A serving gunner was admitted with a minor pyrexial attack and was thought to have had nephritis as the blood pressure was found to be 220/130   He had led a normal life with no symptoms   We were asked to see him because of the widely distributed systolic murmur   The difficult of feeling the femoral pulse (with a blood pressure in the legs of 135/? 85) pointed to the diagnosis of coarctation and this was confirmed by notching of the ribs on X-ray examination   No other evidence of the collateral circulation was seen, but perhaps it was not searched for thoroughly enough   There was no general enlargement of the heart

Case 10, aged 30 (1946)   A doctor consulted us about his high blood pressure which had been found when he was rejected for life insurance four years before   he thought it had been about 150 and once 170, and rather high (135–140) at 21 at a routine examination as a medical student   He knew he had a systolic murmur since childhood and had not been allowed to play football, but had not been short of breath climbing and had led a normal life otherwise   In 1944 he was rejected for the South African Army because his blood pressure was 175/90 and on one occasion 210   his renal function was fully investigated and found to be normal

In 1946 the blood pressure was 210–190/110 in the arms and about 120/80 in the legs   (Subsequently, resting in bed before his operation it was 170/100 in the arms and 100/75 in the legs)   There was a rough systolic murmur in the second and third left intercostal spaces, but no thrill   it was also heard in the back   Apart from rib-notching the only obvious collateral circulation was one artery round the umbilicus (which had probably been mistaken for a vein) but arterial pulsation was increased in the neck and could also be felt over the left costal margin and below the right scapula   His heart was not enlarged, the left ventricle was a little rounded, but would probably have passed as normal without comment

He has since had a successful operation by Dr Crafoord in Stockholm (October 1946)   No details of this are given as he will presumably be reported by Dr Crafoord   Six months after the operation he was leading a normal life without symptoms and the blood pressure was 160–150/90–85 in the arms and 140–145/? 90–85 in the legs   The systolic murmur had greatly diminished and become quite insignificant   All signs of the superficial collateral circulation had disappeared   he stated that the arterial pulsation round the umbilicus had disappeared within a few days of the operation

Case 11, aged 17 (1946)   A bank clerk was sent to hospital because of the findings at a medical board   He admitted to no symptoms except trifling breathlessness compared with his friends, but his last year at school he had been told there was a murmur and had been stopped playing games   The heart was somewhat enlarged to the left with a rounded left ventricle and with a systolic murmur in the third intercostal space just to the left of the sternum, also well heard in the back, and a diastolic murmur in the aortic area   There was also a very slight systolic thrill at the base   The blood pressure in the arms was 195/100 and 130/90 in the legs   There was striking pulsation in the neck and a collateral circulation round the scapulæ   Radiography showed notching of the ribs and an absence of the aortic knuckle (see Fig 7)

A year later he felt in good health and there was no significant change in the physical signs   The collateral circulation in the back was greatly increased when he bent forward

Case 12, aged 33 (1946)   A Canadian was examined for life assurance before starting work in West Africa   He had led a very active life including boxing, rugger, and ice-hockey without any symptoms, but after completing a battle course in 1943 he was told his blood pressure was too high to continue   In 1946, the forcible pulsation in the neck was very obvious, but the femoral pulse was hard to feel   his blood pressure was 210/95, falling to 185/85 after resting, in the arms, and about 140 in the legs   There was a basal systolic murmur which was also heard in the back, but no thrill was felt   His heart was just enlarged clinically but an X-ray was not available   No collateral circulation was noted, apart from the extreme pulsation in the neck

Case 13, aged 27 (1946)   An ex-soldier, who had served six years and been a physical training instructor part of the time without any symptoms found himself tired in his civilian work as a painter and had occasional headaches   His doctor found a raised blood pressure and referred him to hospital

Although the blood pressure was 195/105 when first seen, and 165/92 as the average of many readings when he was in hospital, the femoral pulse was hard to feel and the blood pressure in the leg was about 130   X-ray confirmed notching of the ribs with some enlargement of the heart (Fig 5) and with difficulty some arterial pulsation could be felt (but not seen) below one scapula   He had a systolic murmur at the base (which could be heard in the back also) but no thrill, and a house-physician and presumably the army doctor had not thought it of any special importance   On careful questioning he admitted that he had had pains in the legs during longer marches in the army   He was re-examined a year later   He felt better but there was change in the physical findings   Bending forward demonstrated an increase in the collateral circulation

Case 14, aged 18 (1946)   A young man was sent by a recruiting medical board because of a systolic murmur   He had had a successful series of operations for hypospadias, and had been sent to hospital about his heart when 16, but no details were available and he had been allowed to continue his work He had played games without any undue dyspnœa

There was a rough systolic murmur at the base with a faint systolic thrill   There was no enlargement of the heart   There was forcible pulsation in the neck and a blood pressure of 165/105 in the arms   the femoral pulse was hard to feel and no blood-pressure reading could be obtained in the legs No collateral circulation could be seen, but abnormal pulsation could be felt at several points Coarctation of the aorta was diagnosed and he was placed in Grade IV

A year later, to our surprise he was found serving in a parachute regiment and was carrying out his duties without symptoms   No enquiries were made as to how he had joined the army   The physical signs were much the same and the blood pressure was 170/110 in the arms and could not be obtained in the legs   Bending down showed up the collateral circulation well   X-ray examination showed a high degree of notching and scalloping of the ribs (see Fig 7) and confirmed the absence of any enlargement of the heart though the left border was a little rounded

Case 15, aged 26 (1947)   This man served in the Navy without symptoms, but was told there was something the matter with his heart when he was demobilized   He was sent to hospital by his factory doctor because of an aortic diastolic murmur   He had a systolic murmur to the left of the sternum with a systolic thrill best felt above the clavicles and a soft aortic diastolic murmur to the right of the sternum   His heart was not enlarged and the B P was 160/105   He had never complained of any symptoms but said that when he was about 9 years old there had been some comment on his heart at school

For some reason he escaped X-ray examination and, although the raised blood pressure with a relatively high diastolic pressure without any enlargement of the heart, together with a poor femoral pulse, made coarctation seem likely, rheumatic aortic incompetence and stenosis was thought *possible* because no evidence of a collateral circulation was found (this was in 1946 before Cases 10–14 were seen)

A year later in discussing the possibility of coarctation, we demonstrated that no collateral circulation could be seen in his back when he was standing erect, but that as soon as he bent forward many small arteries stood out and became most obvious over the back and sides of the chest wall (Fig 1) An X-ray film then confirmed the diagnosis by showing deep notching of several ribs   The heart was not enlarged (m t d 13 5 cm in a chest of 29 cm)   The blood pressure varied between 185/120 and 155/95 in the arms and 110/90 in the legs

MYOCARDIAL TUBERCULOSIS WITH PAROXYSMAL VENTRICULAR TACHYCARDIA

BY

ROBERT SCHNITZER

From the Essex County Hospital, Wanstead

Received April 4, 1947

Tuberculous myocarditis is extremely rare, and even in tuberculous pericarditis it is uncommon   The reason for this is difficult to explain   Since the lungs are a common site of tuberculous infection, one might expect myocardial infection to occur much more frequently It has been suggested that the constant movement of the musculature is not conducive to the lodgement of tubercle bacilli or to the development of tubercles, and that the lactic acid produced by cardiac muscular activity offers some protection against Koch's bacilli (Raviart, 1906)   The following unusual case is reported

CASE RECORDS

A Petty Officer in the French Navy, aged 32, was admitted to hospital in August 1945 He looked extremely ill and slightly cyanosed and complained of severe breathlessness and palpitation

History   He had always enjoyed good health   In 1940, during the evacuation from Dunkirk, he was wounded in the left forearm and subsequently the whole limb had to be amputated and he was fitted with an artificial arm   Soon afterwards he began to complain of tiredness and shortness of breath on the slightest exertion and this was followed by attacks of palpitation   These attacks started and stopped abruptly, and were accompanied by severe dyspnœa, an aching sensation in the amputation stump, and occasionally by slight hæmoptysis He had lost 12 lb in weight within five months and was sent to a sanatorium for further investigation   X-rays of his chest suggested some infiltration in both lungs but were at first not quite typical of tuberculosis, and repeated sputum examination, including cultures, failed to reveal acid-fast bacilli   A bronchogram showed no abnormality   After his discharge from the sanatorium he experienced a severe attack of paroxysmal tachycardia in which he was admitted to hospital twelve hours after the onset

Examination   A youthful looking man, ashen-grey and cyanosed, dyspnœic, and sweating profusely   Temperature 99 4° F , pulse very rapid and regular, respiration 36   Neck veins distended, apex beat in sixth interspace 3 5 cm outside mid-clavicular line, no murmurs Blood pressure 130/80 mm   No clubbing of fingers   Trachea central   A few bronchitic sounds scattered over both lungs, especially over the right mid-zone   Liver not enlarged, spleen not palpable, no œdema

Progress   Quinidine, intramuscularly and orally, and carotid sinus pressure failed to stop the paroxysm and acute pulmonary œdema developed   Morphine had only a limited effect   A cardiogram during this attack showed paroxysmal ventricular tachycardia ($P\ V\ T$) with a ventricular rate of 280–300 a minute, similar but not identical with the paroxysm shown later   X-ray of the chest suggested infiltration in the right lung, and to a lesser degree in the left, and some enlargement of the paratracheal gland   Intravenous injection of 0 5 mg

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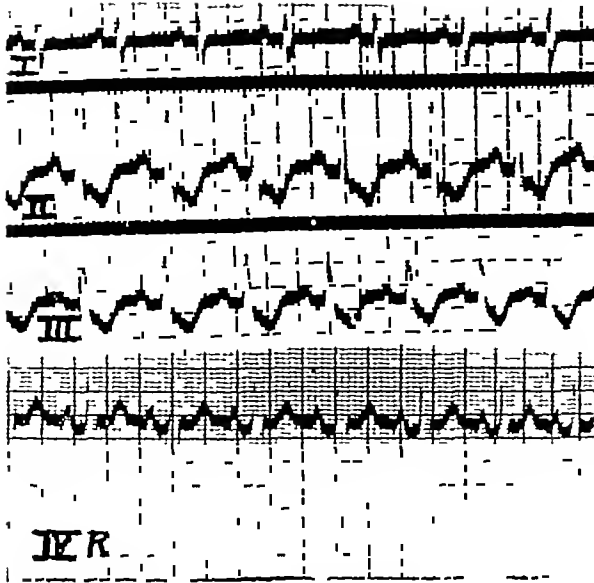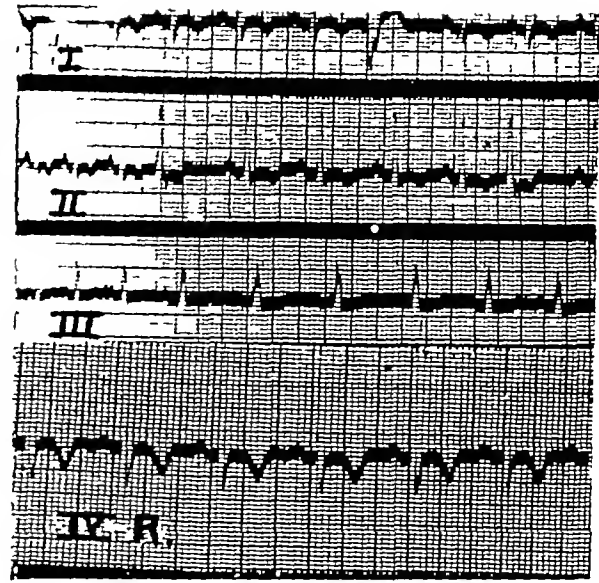
FIG 1

FIG 2

FIG 1 —Electrocardiogram after a paroxysm that lasted 36 hours   Tachycardia ceased after injection of 0 5 mg digoxin intravenously   Changes suggest myocardial infarction of T III type, or possible effect of recent paroxysm, or of digitalis

FIG 2 —Two weeks later   Changes suggest myocardial infarction of T I type
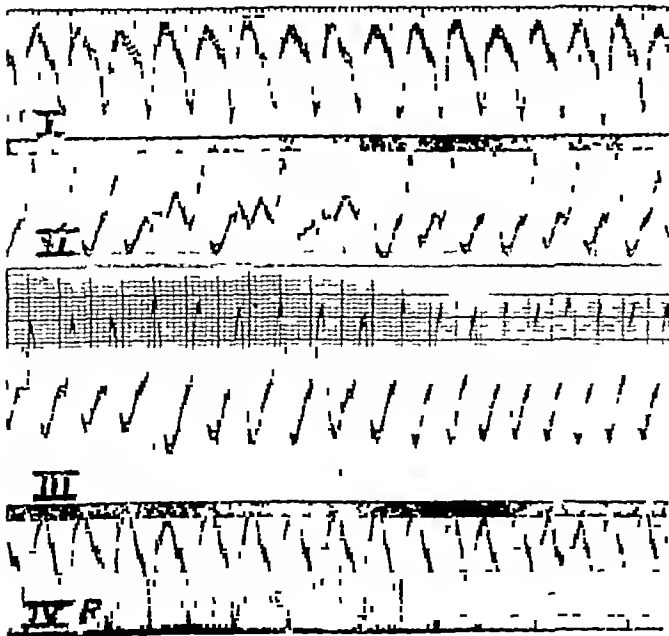
FIG 3
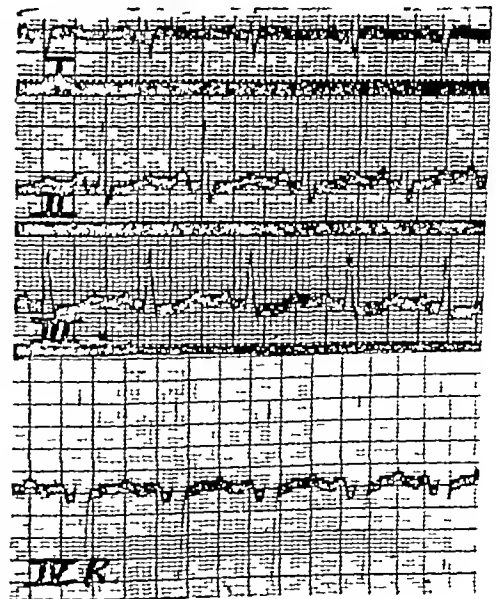
FIG 4

FIG 3 —Paroxysm of ventricular tachycardia that lasted 5 hours

FIG 4 —Ten days before death   Changes seen in the previous tracings have almost completely subsided

digoxin reduced the apex rate to 120, and within one hour a further drop to 108 was observed Digitalis was continued by mouth in small doses and only a few short attacks of *P V T* occurred, but after four days it had to be stopped because of frequent extrasystoles Cardiograms between the attacks showed transient T wave changes which might have been attributed to pulmonary infarction, to posterior cardiac infarction, to the effect of the paroxysmal tachycardia, or to digitalis (Fig 1) Later, however, inversion of the T I suggested anterior cardiac infarction (Fig 2) One night he complained of weakness and a sinking feeling, and tachycardia recurred and persisted until death early the next morning A record of one of his paroxysms of ventricular tachycardia is shown in Fig 3 A cardiogram taken only ten days before his death showed none of the changes seen in previous tracings (Fig 4)

Investigations On admission, white blood cells, 27,700, with 89 per cent polymorphs, 10 days later, 5600, with 71 per cent polymorphs Blood sedimentation rate on admission, 25 mm in one hour (Westergren), 3 weeks later 10 mm in one hour Blood urea 35 mg per 100 ml. Wassermann and Kahn negative Urine, slight traces of albumin with many pus cells, culture sterile Sputum, tubercle bacilli not found, culture for tubercle bacilli negative
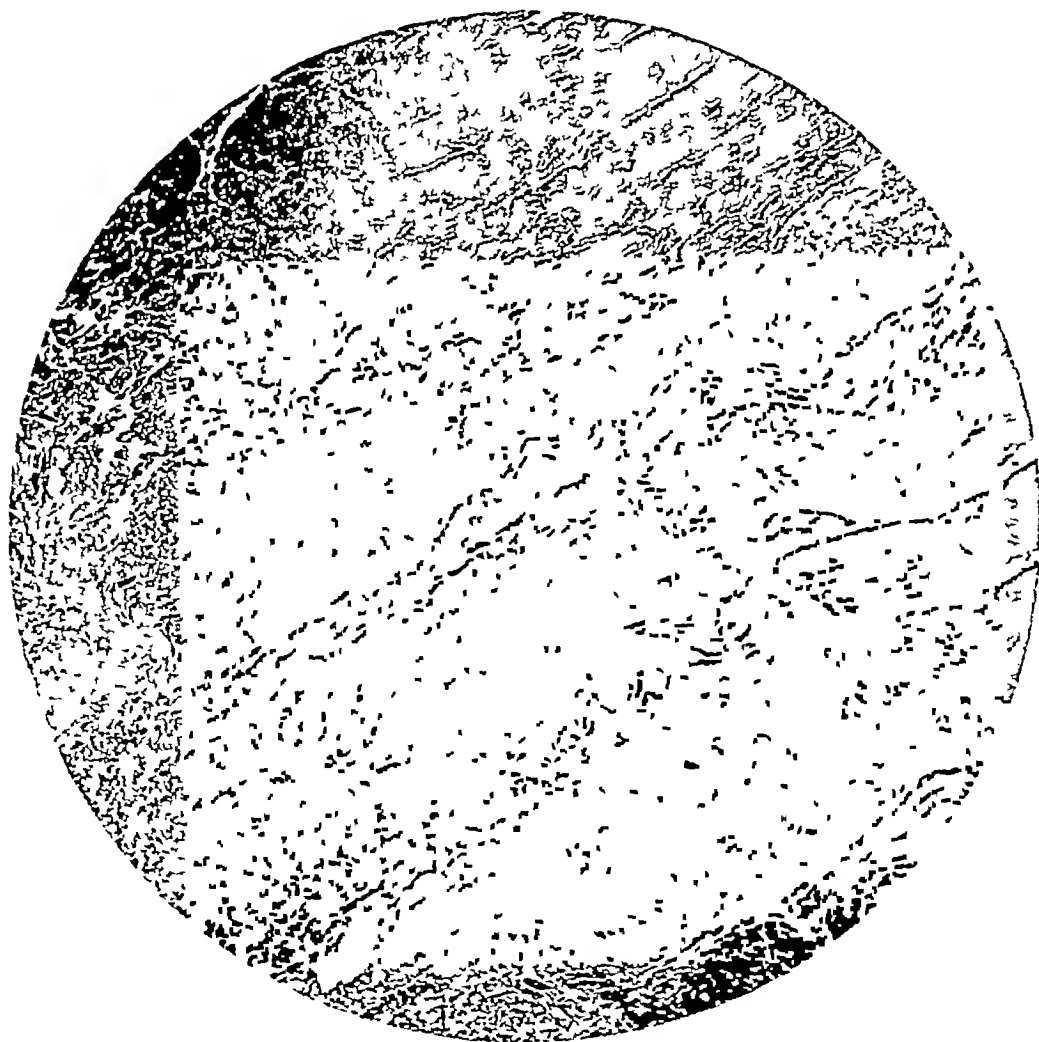
Fig 5 —Section showing giant celled nodules in myocardium Magnification ×52.
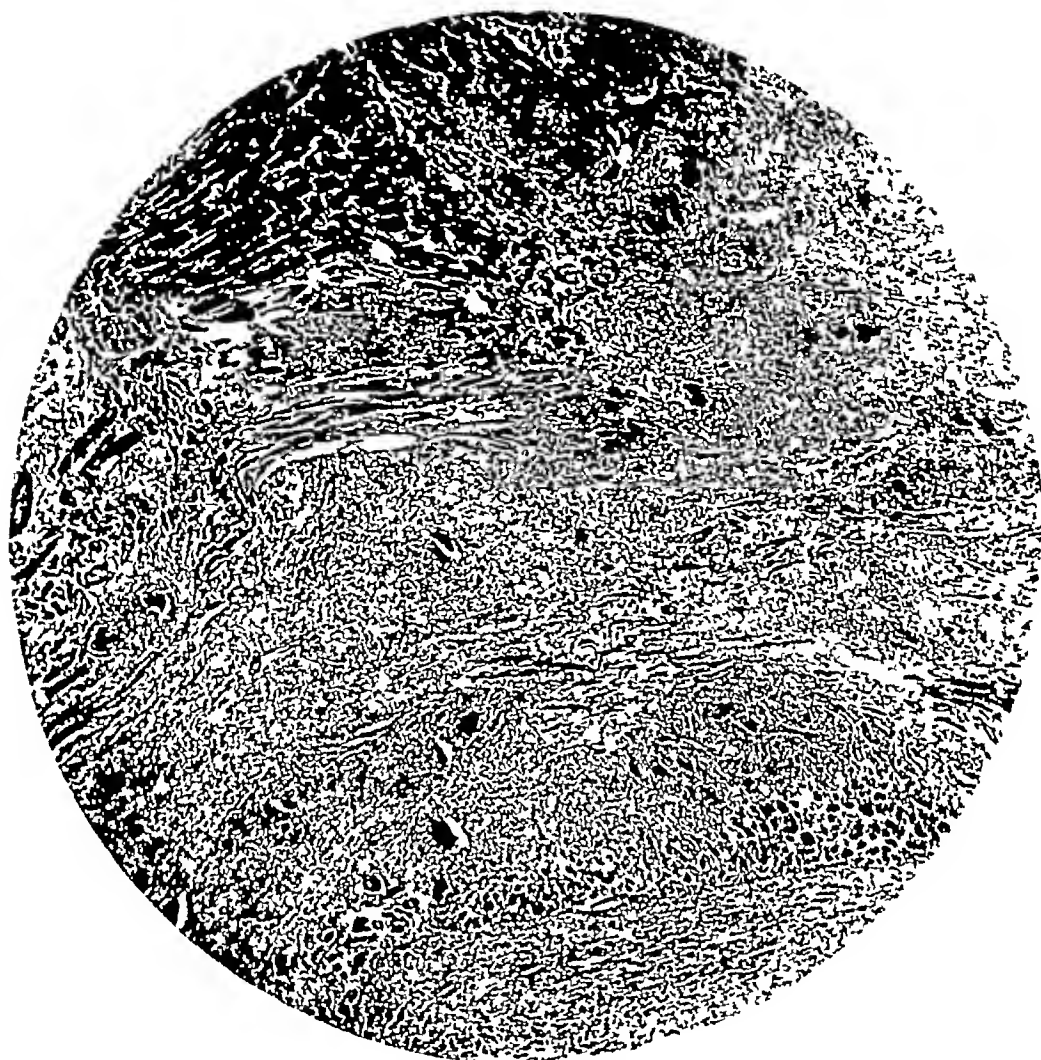
FIG 6 —Section showing confluent caseous tuberculosis, and miliary foci between the lower myocardial fibres   Magnification   ×52

POST-MORTEM EXAMINATION

Heart   There was a small amount of straw-coloured pericardial effusion, but no evidence of pericarditis   There was some enlargement of the heart with slight hypertrophy of the right ventricle   There were multiple greyish and yellowish-grey patches throughout the surface of both ventricles, some had a fibrotic appearance and varied in size from a pea to a shilling   More than half of the anterior wall of the left ventricle was replaced by a uniformly yellowish-grey material which extended upward to the aorta, and the interventricular septum showed two similar smaller lesions   The right coronary artery was patent and free from atherosclerosis, but the anterior descending branch of the left coronary artery was imbedded in yellowish-grey material throughout most of its length and its lumen was almost entirely occluded, though there was no thrombosis   All the valves were normal

Lungs   Paratracheal gland enlarged and firm, the cut surface granular and translucent, its tissue destroyed   There were white patches extending upwards to the lower part of the trachea and downwards into the main bronchi   Multiple greyish-green patches were scattered throughout both lungs, especially in the upper zones   No cavities were seen

The spleen was enlarged and soft, with multiple irregular greyish patches on the surface and in the parenchyma   The liver was not enlarged, but showed similar lesions and a few dark hæmorrhagic areas   Kidneys and adrenals were normal

Histological report   Sections of the lung show numerous miliary and confluent tubercles with central caseation in some   Fibrosis is present within and around some isolated tubercles and is marked in the confluent areas, some of which are reduced almost to hyaline scars Tuberculous arteritis is present in one small branch of the pulmonary artery   The remainder of the lung parenchyma shows œdema and congestion, and alveoli are occupied by an eosino-phil coagulum containing free macrophages   A bronchial gland consists of an acellular mass of collagen, enclosing patches of amorphous debris and cholesterol crystals and surrounded by a capsule of fibrotic granulation tissue containing miliary tubercles

Blocks from the left ventricle and interventricular septum of the heart show similar miliary and confluent miliary tubercles in the myocardium with fibrosis within and around the tubercles   In the left ventricle, fibrous granulation tissue containing tubercles replaces the outer part of the myocardium for a depth of at least 1 cm except for a few included groups of muscle fibres (Fig 5 and 6)   Inflammatory infiltration is slight in this confluent area, and consists of macrophages, lymphocytes, plasma cells, and a few neutrophil leucocytes

The dark areas in the liver proved to be cavernous hæmangiomata and in one section measured up to 1 5 cm in diameter   The remainder of the liver in sections shows albuminous degeneration of the parenchymal cells and scattered miliary tubercles, one having a caseous centre   The spleen shows miliary and confluent miliary tubercles involving Malpighian bodies   The kidneys show albuminous degeneration of the tubular epithelium

The tubercles in the lung, liver, spleen, and myocardium are composed of collagen, epi-thelioid and multinuclear giant histiocytes, fibroblasts, and a few lymphocytes   In many tubercles, most or all of the cells are necrosed, and in some the necrosed cells form a homo-geneous caseous mass   Caseation affects only a part, usually central, of a tubercle   The giant cells are variable in appearance, some are typical Langhans's cells, but others are more of the foreign body type in that the nuclei, of which there are as many as 40, are scattered and chiefly central   In all sites some giant cells contain eosinophil, crystalloid, star-like, radial cytoplasmic inclusions similar to, but probably not so well developed as, those in the Stengel-Wolbach disease   Acid-fast bacilli could not be found in spite of prolonged search   The presence of caseation in many of the tubercles indicates almost certainly that the condition is tuberculous   The absence of tubercle bacilli might be expected in a tuberculous inflammation of such low grade intensity as was evident in this case

DISCUSSION

In the case described, the diagnosis of myocardial tuberculosis is established beyond doubt by the histological findings, despite the absence of tubercle bacilli from the sputum and from tissue sections   The route of infection is difficult to explain in the absence of pericarditis, though the lesions in the paratracheal gland, the bronchi and lungs, suggest a primary lymphatic spread   The tubercle bacilli may have gained access to the venous blood stream via the lymphatic duct, then infected the lungs and eventually entered the general circulation via the pulmonary capillaries, whence the myocardium, liver, and spleen became involved

A case of myocardial tuberculosis was reported by Townsend (1832) who described " a tumour-like auricular growth "   In Anders's (1902) extensive review of the subject, the total of reported cases was brought up to 72   From the time of Bollinger's report in 1890 and Raviart's study in 1906, 101 cases had been observed over a period of 16 years, while only 79 cases had been recognized previously   Norris (1904), in a study of 1764 hearts of tuberculous subjects, observed only 6 cases

Tuberculosis of the myocardium is almost invariably secondary to a tuberculous focus

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elsewhere   In the pathogenesis of this disease, three possible routes of infection have been considered, (*a*) by the blood stream, (*b*) by retrograde lymph extension, and (*c*) by contiguous tissues   Myocardial involvement is usually *secondary to tuberculous pericarditis*   Caseous tuberculous mediastinal lymph nodes, particularly the bronchial or paratracheal group, may be the source of infection of the pericardium and heart   Infection may occur by means of direct contact or through the lymphatics, this latter would necessitate a reversal of the lymph flow, since the drainage of the pericardium has been shown to be upwards into the bronchial lymph nodes (Recklinghausen, 1885)   Another possible mode of spread is by direct extension from the pleura

Three types of myocardial tuberculosis are usually recognized, the nodular, the miliary, and the diffuse infiltrating form   Raviart described a fourth type which he called " chronic interstitial tuberculous myocarditis ", this included the so-called " sclerosis of the myocardium "   The existence of this last form has been disputed and it is generally held that fibrous myocardial lesions which may be found in the hearts of those dying from tuberculosis are not necessarily of tuberculous origin   Some such cases, in which tubercles or tubercle bacilli have been found in sections, probably belong to the diffuse infiltrative form of myocardial tuberculosis   The nodular variety is the commonest, and nodules varying from the size of a pea to that of an egg have been reported   Next in frequency is the miliary variety and rarest is the diffuse infiltrative form   According to Moenckeberg (1924), the last mentioned is a " specific diffuse productive tuberculous myocarditis " most frequently a sequel to pericarditis   Here the myocardium appears to be taken up by a uniformly grey or yellow-grey firm material, which may almost entirely replace the muscle in the areas involved   Most authors report that Ziehl-Neelsen staining has failed to reveal tubercle bacilli in spite of typical histological changes   The infiltrating type most often involves the auricles and may cause auricular extrasystoles and rarely auricular fibrillation (Sweeney, 1940)   The ventricles are sometimes involved, and occasionally extensive destruction of the myocardium and conducting tissues has been observed   Caseous infiltration may destroy half or more of the thickness of the ventricular wall   Coronary occlusion is seldom observed in cases of tuberculosis, and tuberculous arteritis has been observed very rarely in the coronary arteries where it is usually confined to the smaller branches   In one reported case, however, a comparatively large coronary branch was involved, and, in the present case, almost the whole length of the left descending coronary artery was surrounded and partly occluded by tuberculous infiltration   The initial leucocytosis of 27,700, which disappeared within 10 days, may have been due to the ventricular tachycardia rather than to coronary occlusion, for a leucocytosis of 20,000 to 30,000 which subsides rapidly after termination of the paroxysm may be a feature of paroxysmal tachycardia (Levine and Golden, 1922)

SUMMARY

A case of myocardial tuberculosis complicated by paroxysmal ventricular tachycardia is reported   X rays showed pulmonary infiltration, but sputum tests for tubercle bacilli were negative

Necropsy showed miliary tuberculosis with extensive involvement of the myocardium, including the interventricular septum, without pericarditis   The tuberculous nature of the lesions in the heart and other organs was established by the histological findings, which are described

The publications relating to tuberculous myocarditis are briefly reviewed and the pathology is discussed

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Cardiovascular Catheterization as an Aid in Diagnosis of Abnormal Cardiovascular Communications A J GEIGER, H C ANDERSON, A W WINKLER, and H S KAPLAN *Con Med J*, 10, 895–899, Nov, 1946

These authors have applied cardiovascular catheterization to the study of cases of suspected arteriovenous shunts and cardiac septal defects In their interesting paper they give a preliminary account of the procedure in 16 patients Their method is that used by Cournand and Ranges since 1941 in the United States Detailed results obtained by this investigation in 5 cases of suspected abnormal cardiovascular communications are given

The intracardiac catheterization permits (1) direct visualization of the septal defect when the tube passes through the defective septum and into the left heart chambers and their vessels, (2) localized injections of contrast media, such as ' diodrast " in 70% concentration injected with utmost speed and in volumes of 20 to 40 ml , (3) direct-pressure measurements which will give evidence of the shunt through transmission of the relatively high systemic blood pressure to the pulmonary artery or the right ventricle, and (4) removal of blood for gas-content analyses, especially estimation of the oxygen content in samples of blood collected from the respective right heart chambers and vessels In cases of interauricular septal defects the diagnosis is unequivocally established by the finding of considerably oxygenated blood in the right auricle and the passage of the catheter into the right inferior pulmonary vein by way of the left auricle (Case 3)

According to the authors, cardiovascular catheterization is a fairly simple and quite safe procedure which can be conveniently performed even in an out-patient department Except for an occasional local venous thrombosis in the catheterized arm, no untoward effect has resulted No murmurs were heard on auscultation when the catheter had passed through the tricuspid and pulmonary openings Attention is drawn to an occasional failure to demonstrate relatively arterialized blood in the presence of a small septal defect, this happens because (1) a small quantity of arterialized blood is shunted, and (2) the tip of the catheter may be situated out of the line of flow of the shunted blood *A J Suchecki*

Primary Pulmonary Hypertension J R GILMOUR and W EVANS *J Path Bact*, 58, 687–697, Oct, 1946

Clinical observation in a case of cardiac failure had suggested the diagnosis of pulmonary hypertension, and this was confirmed at necropsy A woman of 44 had suffered for 2 years from intense fatigue, dyspnœa on slight exertion, and œdema, and had responded to treatment with rest, digitalis, and mercurial diuretics Diagnoses of hypertensive heart failure and of pericardial disease, respectively, had been made at the 2 hospitals to which the patient had been admitted previously, but the skiagram and the electrocardiogram pointed to a pulmonary-vascular origin of the condition, the first showing enlargement of the right auricle, of the conus of the right ventricle, and of the pulmonary artery, and the latter right ventricular preponderance with an inversion of the T wave in leads II and III and CR$_1$ Although the patient appeared to be responding well to treatment, she died suddenly

At the post-mortem examination there was evidence of congestion in lungs, liver, spleen, and kidneys, there were hypertrophy and dilatation of the right ventricle, dilatation of the right auricle, and adherent thrombi in the right auricular appendage, with slight atheroma in the aorta and " many small flecks of atheroma in pulmonary artery and its branches " The histological examination of the pulmonary vessels showed in numerous sections aplasia or hypoplasia of the media of many vessels, together with intimal changes resembling those of systemic hypertension in these areas, so that stenosis or occlusion of these vessels resulted The deficiency of the media in numerous vessels throughout the lungs was, in the opinion of the authors, the basis for the development of the endarteritis, which occurred as a reaction to transient hypertension, such as might have been produced by coughing and thus started a vicious circle which made the hypertension permanent
B Samet

Parenteral Vitamin B as Agent for Determining the Arm-to-Tongue Circulation Time Part I R E SWENSON *Amer Heart J*, 32, 612–616, Nov, 1946

A commercial preparation of the vitamin-B complex is used to measure the arm-to-tongue circulation time, 5 ml of the preparation being injected intravenously through a No 20 needle, the end-point is given by a sudden, intense, and unique taste sensa ion A duplicate determination can be made within a few seconds of the first one and no untoward complications have occurred *H E Holling*

Tachycardia due to Venous Hypertension in Man (A Study of the Bainbridge Reflex.) La tachycardie créée par l hypertension veineuse chez l'homme (Étude du réflexe de Bainbridge) J LEQUIME, M SEGERS, and H DENOLIN *Acta cardiol*, 1, 1–13, 1946

The authors present the results of the following experiments in support of the hypothesis that an

increased venous pressure leads to a rise of pulse rate (Bainbridge reflex) in man, and that this is mediated by the vagus nerve   In the course of the investigations a proportion of the subjects showed an increased respiratory rate when the venous pressure was raised —an effect similar to that observed by Harrison in animals   It is emphasized that the Bainbridge reflex cannot completely account for the cardiac acceleration after exercise

Eleven subjects were infused with 1 litre of warmed serum over a period of 5 to 10 minutes   The venous pressure was found to rise 12 to 24 mm of water Electrocardiographic records taken over the same period showed an increased pulse rate of 8 to 25% After 4 subjects were given 2 mg of atropine intravenously the pulse quickened and the venous pressure fell   Infusions were then administered as before without influencing the heart rate, though the venous pressure rose above resting levels   (During the course of all these investigations there was no change of blood pressure as measured by a Pachon oscillometer) In a case of femoral arteriovenous aneurysm, compression of the anastomosis gave a fall of venous pressure and pulse rate and a rise of arterial pressure as measured directly by a cannula in the opposite femoral artery   These changes were suppressed after the administration of 1 5 mg of atropine intravenously   The respiratory rate was observed to increase after infusion in 8 of the 11 subjects   (The vital capacity remained constant)   This effect was not observed when atropine was administered first It was not seen in the arteriovenous aneurysm   The possibility that some of these effects might be due to transfusion reactions, or to pharmacological substances in the serum used, is not discussed

W J H Butterfield

Hypertension and Calcium Intake   C M KESSON and A McCUTCHEON   *Lancet*, 2, 793, Nov 30, 1946

The authors, in the Stobhill Hospital, Glasgow, have studied a group of 80 patients over the age of 40 years to see whether any correlation exists between osteoporosis and arteriosclerosis   In 30 there was evidence of osteoporosis, and in these the blood pressures were similar to those of the control cases, while arteriosclerosis and arterial calcification were present equally in the two groups   In subsequent investigations which entailed a daily calcium intake of 1 6 g for periods of 6 to 15 months no hypertension developed and arterial calcification did not progress   It is concluded that, contrary to the claim of Harris, a high-calcium diet over many months has no effect on the development of arteriosclerosis

R Bodley Scott

Clinical Aspect of Polyarteritis Nodosa   H G MILLER and R DALEY   *Quart J Med*, 15, 255–283, Oct , 1946

Though more cases of polyarteritis nodosa than formerly are now being recognized before death, a large proportion are still missed   The authors believe

that the difficulty of diagnosis during life is only in part inherent in the behaviour of the disease, and that in many cases it is due either to failure to consider the diagnosis in a difficult case or to rejection of the diagnosis, once considered, because of the absence of one or more signs, such as subcutaneous nodules or eosinophilia, which are considered typical but are actually of infrequent occurrence

To clarify the clinical picture, so far as is possible in a condition of such protean manifestations, the more important past writings are reviewed and 9 new cases are recorded.   *R T Grant*

Dissecting Aneurysm of the Aorta   (A Study of a Series of Fourteen Cases)   J D PALMER and A K MATHISEN   *Canad med Ass J*, 55, 585–595, Dec , 1946

Ante-mortem diagnosis of dissecting aneurysm of the aorta is difficult   The patient usually dies of rupture of the aneurysm with a massive hæmorrhage, but occasionally he may survive and organization and obliteration of the sac or rupture back into the lumen may occur with formation of a double-barrelled aorta The incidence in the Royal Victoria Hospital, Montreal, was 1 in 575 necropsies, compared with 1 in 175 reported by Shennan   There were 7 male and 7 female patients, whose average age was 49 years Onset of symptoms was sudden and occurred when the patient was at rest   severe pain is felt in the præcordial region or upper quadrants of the abdomen, or, if the dissection involves the abdominal aorta, may spread into the lower abdomen, and it later spreads into the back   Pain is intense, sharp, and tearing and may recur   All patients show marked prostration and signs of shock may be present   In 8 cases the blood pressure was high on admission, while in 8 it was low   Temperature was normal on admission, but in those who survived the temperature rose after the first day to 100°–101° F   (37 8°–38 4° C) White-cell count and erythrocyte sedimentation rate were moderately raised   In most cases the urine contained albumin, hyaline casts, and red cells   In two cases hemiplegia resulted from involvement of the orifice of the innominate or carotid artery   The Wassermann reaction was usually negative, and the chest radiography revealed widening of the arch of the aorta   Electrocardiograms in 10 cases showed the changes of hypertensive heart disease, where previous records were available no change since the incident could be found.   In 1 case electrocardiographic changes like those of coronary occlusion appeared on the tenth day, and necropsy disclosed involvement of the coronary arteries by the dissection, and the presence of blood in the thoracic cavity, usually on the left side   In 2 instances there was blood in the pericardium   The ascending and transverse portions of the arch were most commonly affected   The aorta showed medial necrosis and the heart was hypertrophied in all cases except one   It is considered that hypertension was an important factor in the production of the dissection

J McMichael

Hypertrophy of the Heart of Unknown Etiology in Young Adults   Report of Four Cases with Autopsies R F NORRIS and H H POTE   *Amer Heart J*, 32, 599–611, Nov , 1946

Death from congestive heart failure occurred in four instances of unexplained cardiac hypertrophy and dilatation   These 4 unusual cases occurred during 1 year at the Philadelphia Naval Hospital, and the victims were all sailors between the ages of 21 and 30 years   The cardiac hypertrophy was in all cases recognized and investigated some time before death, so that the usual causes of the condition had been excluded   It would have been more satisfying, as the authors point out, if glycogen-storage disease could have been excluded   There was, of course, no indication that the ætiology was the same in all 4 cases

H E Holling

Anoxemia and Exercise Tests in the Diagnosis of Coronary Disease G BIÖRCK   *Amer Heart J*, 32, 689–696, Dec , 1946

This contains a discussion of the value of the various tests designed to elicit anginal pain or electrocardiographic changes in patients in whom the diagnosis of coronary artery disease is in doubt   The general conclusion is that such tests are not to be recommended for general use, their application and interpretation require considerable experience and they are liable to provoke unpleasant reactions   *R T Grant*

Notes on the Similarity of QRS Complex Configurations in the Wolff-Parkinson-White Syndrome G E BURCH and J L KIMBALL   *Amer Heart J*, 32, 560–570, Nov , 1946

From a review of the literature the authors conclude that the various configurations of the QRS complex seen in the electrocardiograms of cases of Wolff-Parkinson-White syndrome may be classified into 5 types   The criteria employed in diagnosis were (1) a short P–R interval and a prolongation of the QRS duration with slurring and notching, (2) absence of any clinical signs of heart disease in most instances, (3) repeated paroxysms of tachycardia, and (4) return of the electrocardiogram to normal on parasympathetic depression and exercise as well as spontaneously   The similarity of types III and IV to left and right bundle-branch block is pointed out, the short P–R interval indicating the correct diagnosis

The Wolff-Parkinson-White syndrome is due to the existence of an anomalous conducting pathway connecting the auricles to the base of the ventricles   Impulses from the auricles pass down this pathway as well as by way of the auriculo-ventricular node and Purkinje system, but owing to the shorter course of the anomalous pathway the process of ventricular depolarization is initiated earlier in the region around its termination   The site of termination of this pathway is an important factor in the configuration of the electrocardiogram   *B McArdle*

Electrocardiographic Changes occurring during Treatment with Fuadin Solution S B BEASER and R RODRIGUEZ-MOLINA   *Amer Heart J*, 32, 634–644, Nov , 1946

The authors report that 20 of 25 cases receiving fouadin treatment for infections with *Schistosoma mansoni* showed decrease in the voltage of the T waves of the electrocardiogram   These changes were reversible after 3 or more weeks   It is suggested that the drug affects the myocardium, and that courses of therapy with it should be separated by a similar period to prevent cumulative effects on the myocardium

W J H Butterfield

Orthostatic Paroxysmal Ventricular Tachycardia M PETERS and S L PENNER   *Amer Heart J*, 32, 645–652, Nov , 1946

The authors describe the case of a woman, aged 24 years, who for 1½ years had had frequent attacks of tachycardia occurring only in the upright position, always ending when she lay down, and recurring on standing   Electrocardiograms taken during attacks were characteristic of paroxysmal ventricular tachycardia   The relation to posture was confirmed   The authors review the literature of paroxysmal ventricular tachycardia and suggest that in their cases the attacks were due to unusually strong sympathetic tone

B McArdle

The Combined Use of Lanatoside C and Quinidine Sulfate in the Abolition of Established Auricular Flutter R M TANDOWSKY, J M OYSTER, and A SILVERGLADE   *Amer Heart J*, 32, 617–633, Nov , 1946

Intravenous lanatoside C (a glycoside of digitalis) was found to be more effective than digitalis (especially when given by mouth) in the conversion of established auricular flutter to fibrillation   An initial dose of 1 6 mg given intravenously was followed by a daily maintenance dosage of 1 mg   Twenty-one cases were treated   Of these, 4 reverted to sinus rhythm within an hour   auricular fibrillation was established in 15 within 2 to 72 hours and in 1 case after 13 days' treatment, while in a thyrotoxic patient (before operation) the rhythm was unchanged   In all but 4, primary slowing of the ventricular rate occurred within an hour   Quinidine sulphate with lanatoside C (1 mg daily) was given to the 15 patients who developed auricular fibrillation   Owing to intolerance the quinidine was discontinued in 1 case, the remaining 14 reverted to sinus rhythm within 1 to 10 days, but flutter recurred immediately the quinidine was discontinued in 1 case, and in 1 other sinus rhythm was followed by nodal tachycardia and sudden death   Necropsy showed an extensive myocardial infarct   The remaining patients received a maintenance dose of lanatoside C over an average follow-up period of 11 months without recurrence of flutter   Lanatoside C is superior to digitalis leaf because of its rapidity of action when given intravenously and its strong vagal action   *B McArdle*

Electrocardiographic Criteria of Bundle-branch Block and its Location (Present Position of the Question) (Les critères électrocardiographiques du bloc de branche et de sa localisation État actuel de la question) H DENOLIN *Acta cardiol*, **1**, 44–68, 1946

This is a good review of the literature of bundle-branch block The author considers that our present criteria for diagnosis of abnormalities of interventricular conduction may prove hazardous, and that the diagnosis of asynchronous contractions of the ventricles may prove particularly so He points out that the duration of the QRS complex may be prolonged to over 0 1 second in healthy hearts, and the position of the heart in the chest and the electrical conductivity of the tissues adjacent to it may cause aberrations of the ventricular complex This being so, he would prefer that electrocardiographs showing a QRS deflexion prolonged over 0 1 to 0 12 second and followed by a T wave of opposite polarity should be judged diagnostic of a " disturbance of intraventricular conduction ", and that the term " bundle-branch block " should not be used because it presupposes a pathological state of the ventricles which may not be otherwise demonstrable He points out the need for further study of asynchronous contraction of the ventricles   *H E Holling*

The Clinical Significance of Certain Changes in the Limb Lead Electrocardiogram in Arterial Hypertension G F FILLEY *Bull Johns Hopk Hosp*, **79**, 261–282, Oct, 1946

The electrocardiogram of left ventricular strain shows inversion of the T waves in lead I or leads I and II with left axis deviation and high voltage The significance of this change is still uncertain The author has analysed the clinical and pathological findings in 100 cases of arterial hypertension with these changes in the electrocardiogram The electrocardiographic changes become most marked with diastolic pressures over 130 mm Hg and in the presence of coronary sclerosis Cases of myocardial infarction were excluded from consideration When the heart weight is above 500 g the electrocardiographic change is also pronounced There was no relation to the predominance of left ventricular over right ventricular hypertrophy as gauged by the ratio of thickness of walls of right and left ventricles or of weights of these chambers

The electrocardiographic changes in themselves do not indicate a very bad prognosis The strain pattern reflects primarily the degree of hypertrophy in response to the high diastolic pressure rather than the state of myocardial sufficiency, it does not seem to bear any relation to the duration of the hypertension The relation of coronary artery disease suggests that the T-wave changes are associated in some way with the myocardial blood supply, and also with hypertrophy The changes of strain, however, should not be interpreted as unfavourable signs They are quickly reversed after sympathectomy   *T McMichael*

The Diagnosis and Treatment of Tracheal and Esophageal Obstruction Due to Congenital Vascular Ring R. H SWEET, C W FINDLAY, and G C REYERSBACH *J Pediat*, **30**, 1–17, Jan, 1947

Two cases of this rare congenital defect due to a double aortic arch are reported The infants developed a persistent cough and inspiratory stridor within two weeks of birth In the first case, radiological examination of the œsophagus with the aid of barium, when the child was 3½ months old, showed an indentation posteriorly at the level of the aortic arch and, slightly below this, another indentation of the right lateral margin of the œsophagus Surgical exploration confirmed the diagnosis, and the ductus arteriosus and ventral component of the double aortic arch were ligated and divided The patient made an uneventful recovery In the second case radiological examination at the age of 2 years showed a displacement of the superior mediastinum to the right and a narrowing of the trachea at the level of the aortic arch posteriorly and on the right Two years later, radioscopy with barium showed an œsophageal deformity at the same level At operation a vessel representing a persistent right fourth aortic arch connecting the ascending and descending aorta was identified, ligated, and divided The subsequent progress of the child was satisfactory   *Jas M Smellie*

The Effect of Anticoagulants on the Penicillin Therapy and the Pathologic Lesion of Subacute Bacterial Endocarditis. W S PRIEST, J M SMITH, and C J McGEE *New Engl J Med*, **235**, 699–706, Nov 14, 1946

It has always seemed logical to use anticoagulants in the treatment of subacute bacterial endocarditis in order not only to prevent the formation of fibrin deposits and to make bacteria more accessible to therapeutic agents but also to diminish the frequency of embolism This communication concerns 34 consecutive cases of bacterial endocarditis treated with penicillin at the Wesley Memorial Hospital, Chicago Of these, 15 received in addition heparin or dicoumarol, either alone or in combination, and 19 were treated without anticoagulants In the entire series there were 12 deaths, 8 of the patients had received anticoagulants at some period of their treatment The authors found that the use of anticoagulants did not always prevent major embolism, and that there was no quantitative difference in the amount of fresh fibrin on the lesions whether anticoagulants had been given or withheld Heparin proved an expensive treatment, not only from its intrinsic cost but also because of the necessary daily tests of prothrombin time The important conclusion reached was that, if the daily dose of penicillin is adequate, healing will take place as well without, as with anticoagulants All 15 of the latest cases recovered with 1,000,000 units or more of penicillin daily Anticoagulants may have been responsible for fatal hæmorrhage in 2 cases   *James W Brown*

Paroxysmal Hypertension   A S ROGEN   *Lancet*, 1, 103, Jan 18, 1947

As evidence that paroxysms of hypertension may be caused by a rapidly growing cerebral tumour, even when it does not invade the thalamus or hypothalamic region, the author records the case of a man of 62 with a few weeks' history of epileptiform attacks, whose origin from a right cerebral focus was shown by twitching of the left arm and leg followed by left hemiparesis and aphasia   There had been no significant headache, giddiness, or papilloedema, but the blood pressure had fluctuated between wide limits (260×/140 and 110/70 mm), the higher reading being associated with his epileptiform attacks, though it was occasionally unrelated to these   Apart from an apparently positive cold pressor test (Hines, *Amer Heart J*, 1940, 19, 408) there was no evidence of an adrenal medullary tumour (phæochromocytoma), though this diagnosis had been seriously enough considered for laparotomy to be contemplated   At necropsy a large glioblastoma was found occupying the right parietal and occipital lobes, this did not encroach on the thalamus or hypothalamus   No adrenal tumour was found
Henry Cohen

2-Thiouracil in the Treatment of Congestive Heart Failure   E P SHARPEY-SCHAFER   *Brit med J*, 2, 888–889, Dec 14, 1946

The theoretical purpose of thyroidectomy in congestive heart failure is to reduce the total oxygen requirements of the body and so decrease the work of the heart   As a means of avoiding the high mortality associated with thyroidectomy in severe cases of cardiac failure the author tried the effect of 1 to 2 g of 2-thiouracil given over long periods   Detailed results of the treatment of 12 cases are presented

By means of cardiac catheterization the cardiac output and right auricular pressure were measured, and the work of the heart was calculated arbitrarily from the product of the cardiac output and the blood pressure   Seven cases of low-cardiac-output heart failure (hypertension and valvular heart disease) and 5 cases of high-cardiac-output failure (emphysema) were treated, and, as several had already received a long period of treatment by ordinary methods, spontaneous improvement was considered unlikely It was found that the basal and resting oxygen consumption were reduced by thiouracil, but it did not follow from this that the cardiac output necessarily fell, as sometimes the arteriovenous oxygen difference decreased with the fall in oxygen consumption   Since the blood pressure sometimes remained unchanged it follows that the work of the heart may be unaffected by thiouracil   Even so, clinical improvement, as judged by a fall in venous pressure and an increase in exercise tolerance, resulted in both groups in the majority of cases   It is pointed out that no benefit can be expected in rapidly deteriorating patients, as thiouracil takes a week or 10 days before its effect on the thyroid is evident   *S Oram*

The Present Status of Penicillin in the Treatment of Subacute Bacterial Endocarditis   H E RYKERT   *Canad med Ass J*, 55, 543–547, Dec , 1946

Fifteen patients with subacute bacterial endocarditis treated with penicillin in the Toronto General Hospital are reported, in 5 the disease was clinically arrested, 5 died of complications (nephritis, 1, emboli, 3, and congestive failure, 1), but in these the infective process was probably arrested, while in another 5 the treatment failed   In one of the failed cases the cause was probably an insensitive strain of streptococcus, but in the others it was difficult to determine the cause of failure   A daily dose of less than 200,000 units is likely to be inadequate   If the response to this is unsatisfactory (blood cultures remaining positive, fever persisting) the dose should be increased to 500,000 units daily   There is little to be gained by any increase above this dosage   The average duration of the disease in the clinically arrested cases was 8 weeks, compared with 23 weeks in the cases in which the treatment failed   Long duration of the disease leads to deep location of the organisms in the vegetations   Either continuous intramuscular drip or interrupted injections are suitable   *J McMichael*

The Esophageal Electrocardiogram in Arrhythmias and Tachycardias   C BUTTERWORTH and A C POINDEXTER   *Amer Heart J*, 32, 681–688, Dec , 1946

This paper emphasizes the value of the œsophageal electrocardiogram in aiding accurate diagnosis in certain cases of tachycardia and arrhythmia   It is of special value in those abnormalities in which the P waves are difficult to identify accurately—as, for example, when the P wave is superimposed on the ventricular complex or when P-wave voltage is low Illustrative electrocardiograms are given   The construction and use of œsophageal electrodes are briefly described   *R T Grant*

Electrocardiogram in Derangements of the Organism's Water and Electrolyte Metabolism   [In English] O J BROCH   *Acta med Scand*, 126, 157–176, Nov 9, 1946

Electrocardiograms were taken on 18 patients with well-marked dehydration or disturbance of acid-base or electrolyte balance   Dehydration (determined clinically or by changes in hæmoglobin concentration) was usually associated with a depression of the S–T interval in one or more leads, but there was no correlation between the degree of this depression and the severity of the dehydration   The S–T interval became isoelectric on restoring the fluid balance, but the T waves usually became temporarily flattened or diphasic for 1 to 3 weeks   The author believes that these changes were due to an inadequate coronary blood flow secondary to the dehydration   Potassium chloride given as a 25% solution to 4 cases of renal insufficiency caused a rise in the height of the T waves when these were positive, or a smaller deflection when negative   *B McArdle*

HEART MURMURS

PART II

BY

WILLIAM EVANS

From the Cardiac Department of the London Hospital

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A phonocardiographic study of the innocent heart murmurs and those found in mitral stenosis was described in an earlier publication (*Brit Heart J*, 1947, 9, 1)   In this paper the murmurs appearing in aortic valvular disease, hypertension, congenital heart disease, heart block, and in anæmia are examined

III THE MURMURS OF AORTIC VALVULAR DISEASE

The finding of a systolic murmur in the mitral area in patients with disease of the aortic valve is commonplace   Often it is difficult on clinical grounds to decide the source of the mitral murmur, whether it comes from the aortic valve, whether it is caused by the hyper-trophied left ventricle, or whether it arises from associated disease of the mitral valve   Indeed, so loud is the mitral murmur in many patients with aortic valvular disease, especially stenosis, that it has seemed natural to assume that the mitral valve is also affected, cardioscopy has then been applied to decide whether mitral stenosis accompanied it or not, but often this examination has been inconclusive

A phonocardiogram was recorded in 40 cases of aortic valvular disease from the mitral area for it was to the elucidation of the mitral systolic murmur that the investigation was primarily directed   Often a record was taken from the aortic area as well, but as it added no exceptional information, routine recording in this area was not pursued   Among the 40 cases there were 10 with aortic stenosis, 20 with aortic incompetence, and 10 with probably aortic valve sclerosis   The phonocardiographic findings in each group will be described in turn

AORTIC STENOSIS

Not all the cases of aortic stenosis showed a thrill, but each had a loud and rough systolic murmur both in the aortic and mitral areas   The presence or absence of diastolic murmurs in both these areas was noted   The electrocardiogram was often abnormal, on cardioscopy a varying degree of left ventricular enlargement was found, and as a rule the aortic shadow was abnormal, commonly from unfolding of the aorta

The mitral systolic murmur in the phonocardiogram started at the S line in five cases, immediately after the S line in three, and a little later in another (Fig 21 and 22)   In one case where the murmur started before the S line there was a mid-diastolic murmur as proof of the association of mitral stenosis   The systolic murmur always continued up to or within a short distance of the second heart sound

In 2 of the 10 cases an early diastolic murmur of aortic incompetence was heard with the stethoscope although the systolic murmur was more in evidence   The remaining 8 were regarded as uncomplicated aortic stenosis because the murmur of incompetence had not been found although it had been sought diligently by direct auscultation during halted respiration

T   225
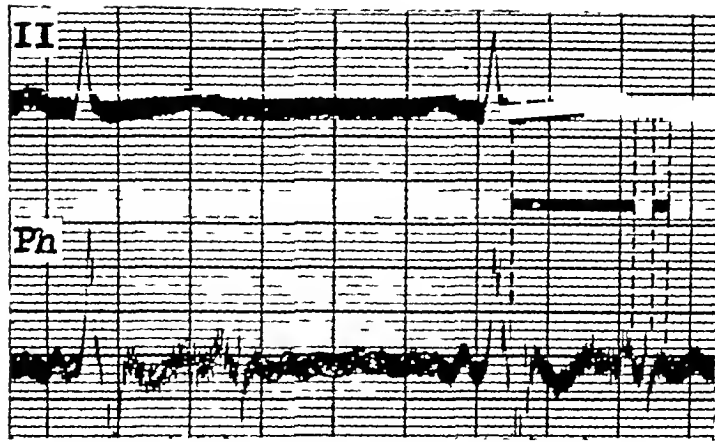
FIG 21 —Aortic stenosis The systolic murmur starts at the S
line, and a diastolic murmur following the second heart
sound is evidence of accompanying aortic incompetence
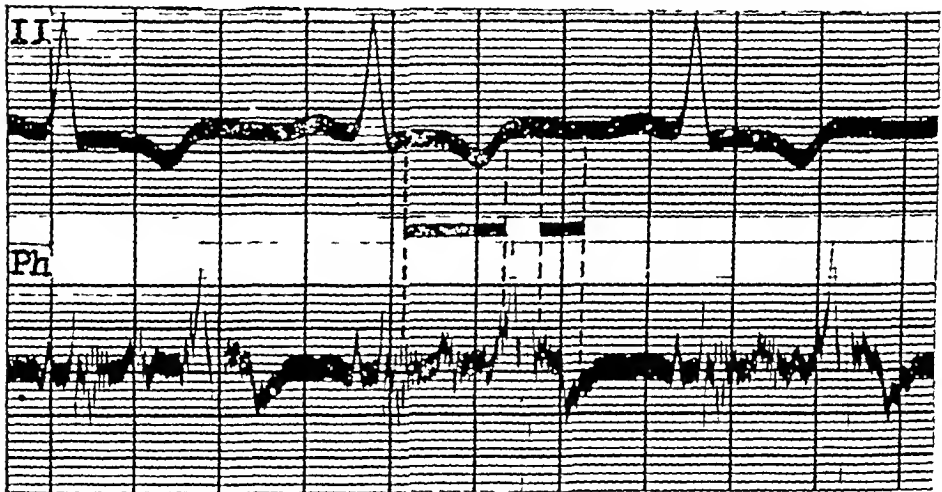
FIG 22 —Aortic stenosis The systolic murmur starts a little later than the S line
A diastolic murmur follows the second heart sound, giving proof of aortic
incompetence, although this murmur was not heard on auscultation

and with the patient in the upright posture, yet in all eight of them a murmur immediately
following the second heart sound was recorded in the phonocardiogram proving the presence
of aortic incompetence

AORTIC INCOMPETENCE

There were 20 cases of aortic incompetence in which a rheumatic origin could not be
substantiated on clinical grounds although the comparative youthfulness of five supported
that ætiology   Radiological examination too could not establish definitely the presence of
mitral disease, in the right oblique position the left auricular impression was usually prominent
but it was difficult to tell with certainty whether this was caused by a displacement backwards
of a normal left auricle due to the enlarged left ventricle, or caused by a left auricle distended
from mitral disease

In 8 cases the aortic incompetence was considered to be of syphilitic origin, but in 4 of
these the phonocardiogram showed auricular and mid-diastolic murmurs proving a rheu-
matic ætiology   In all these 8 cases an Austin Flint murmur had been suspected by others,

but in the 4 where the sound record proved the presence of mitral stenosis the murmur was evidently a true presystolic murmur   Of the other 4 cases with alleged Austin Flint murmur the phonocardiogram showed nothing distinctive in two apart from the early diastolic murmur, and neither auricular nor ventricular moieties of the first heart sound showed anything odd (Fig 23)   In two cases where the aortic regurgitation was free the murmur lasted throughout diastole and was continued into systole (Fig 24)   In these four non-rheumatic cases the systolic murmur commenced at the S line (Fig 25)

In the 12 cases where the aortic incompetence was considered to be non-luetic, there was no clinical evidence of mitral disease that would have suggested a rheumatic origin for the aortic lesion, but in every instance the phonocardiogram supplied such a proof, demonstrating both auricular and mid-diastolic murmurs   It is true that in two patients, aged 17, and in three, aged 26, 28, and 28 years respectively, a rheumatic aortic incompetence had been presumed because of their age, but the phonocardiographic test gave the proof
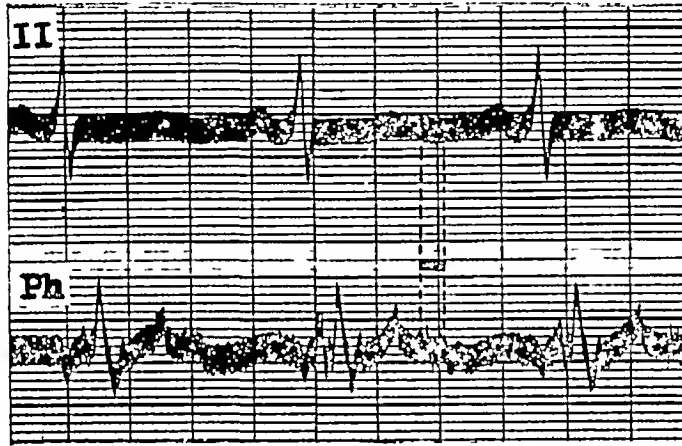
Fig 23 —Luetic aortic incompetence   A diastolic murmur accompanies the second heart sound   Although three observers told of the presence of an Austin Flint murmur on auscultation the auricular and ventricular moieties of the first heart sound show nothing distinctive
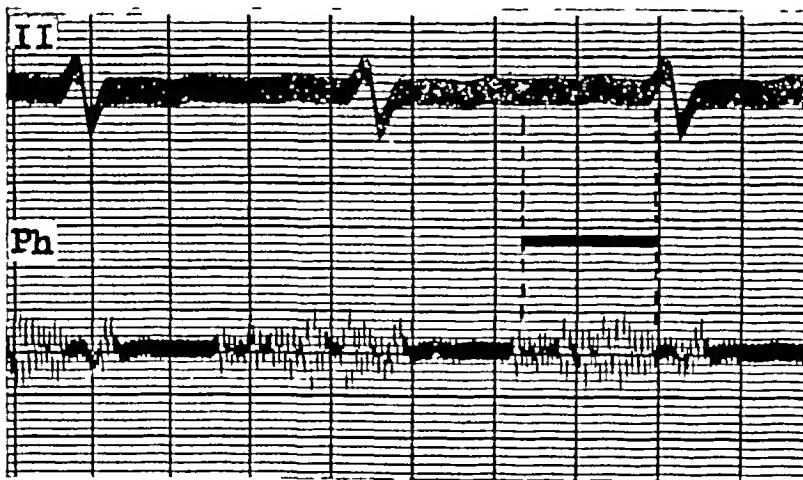
Fig 24 —Aortic incompetence luetic in origin and of considerable degree The diastolic murmur starts at the second heart sound and is continued through the whole of diastole into systole
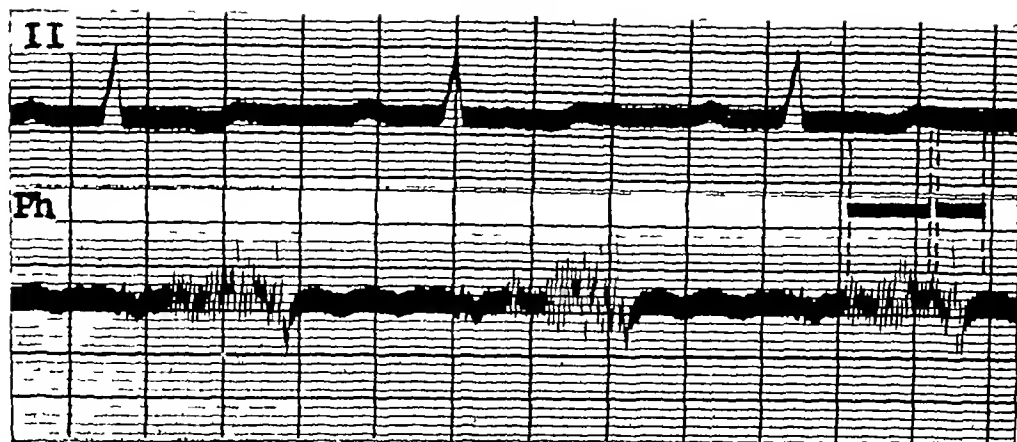
FIG 25 —Aortic incompetence   The systolic murmur in this case starts in mid-systole some distance after the S line

The early diastolic murmur was always recorded immediately after the second heart sound, and although variable in its duration, it was usually short and had spent itself mostly when the third heart sound was reached, except when the regurgitation was prominent it lasted throughout diastole to reach auricular systole   In this event the phonocardiogram cannot help to decide the ætiology of aortic incompetence, it is only when the early diastolic murmur has stopped short of auricular systole that an auricular systolic murmur will indicate mitral stenosis, and should it stop short of the third heart sound a mid-diastolic murmur is added as a sign of mitral stenosis

It is likely that the phonocardiograph, when it comes into routine use, will often reveal an undiscovered aortic incompetence by recording the early diastolic murmur (Fig 26), although when the test has shown it to be present, careful re-auscultation should discover the murmur
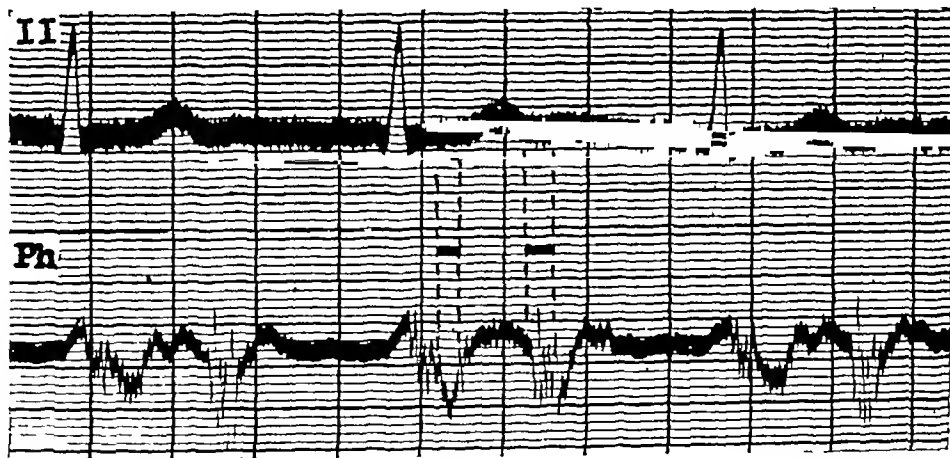
FIG 26 —Early aortic incompetence   Clinical examination had concluded that a systolic murmur was of the innocent kind, but the phonocardiogram showed an early diastolic murmur   Subsequent examination by direct auscultation easily confirmed the presence of this murmur

Having noticed the frequency in elderly subjects of a mitral systolic murmur where an aortic systolic murmur is heard best or only heard in the upright posture on direct auscultation and unaccompanied by a thrill, I collected 36 such cases   The cause of the murmur seemed to

be a benign one, and so it proved in two of the patients when examined at necropsy, in one, death had resulted from carcinoma of the bronchus, and in the other, from an unusual form of anæmia   The aortic cusps in both cases showed bars of thickening at their bases by calcareous atheroma which had spread from the aorta on to the aortic aspect of the cusps, producing a sub-clinical stage of aortic stenosis (*aortic valve sclerosis*)   A phonocardiogram was recorded in the mitral area in 10 such cases   In 6 the systolic murmur started at the S line as it had done in most patients with aortic stenosis and aortic incompetence, but in the remaining 4 it was postponed until mid-systole (Fig 27)   In 6 cases the murmur stopped short of the second
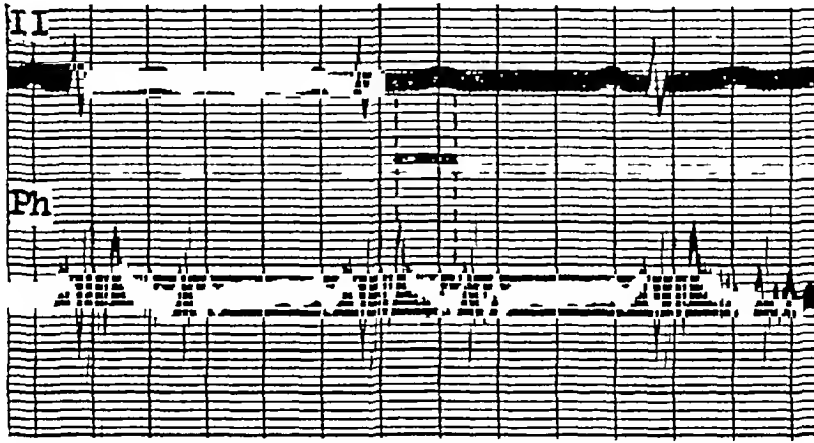
FIG 27 —Aortic valvular sclerosis   The systolic murmur in this case starts
in mid-systole a short distance beyond the S line

heart sound, and in this respect it differed from the systolic murmur of aortic stenosis and incompetence which reached the second heart sound

SUMMARY   MURMURS OF AORTIC DISEASE

The phonocardiographic investigation of murmurs heard in the mitral area in *aortic stenosis* has shown that the clinical diagnosis may have to be corrected in two ways   First, the commoner revision applied to the additional diagnosis of aortic incompetence when this has gone unsuspected by auscultation, this added finding was present in the phonocardiogram in every case in this series as it happened, but I have found exceptions since   Secondly, when aortic valvular disease had been regarded as a lone lesion the phonocardiogram twice showed auricular and mid-diastolic murmurs at the apex proving that mitral stenosis was present Whenever the aortic lesion existed alone the systolic murmur usually started at the S line which marks the commencement of ventricular systole

In the case of *aortic incompetence* the phonocardiogram frequently demonstrated the presence of mitral stenosis where this had gone unrecognized on clinical and radiological examination   In half the cases where the aortic incompetence was believed to be luetic in origin and showed a murmur that might be described as Austin Flint, the sound tracing showed it was a presystolic murmur of mitral stenosis, in the other half the sound record either showed no change in the auricular or ventricular moieties of the first heart sound, or the early diastolic murmur had lasted throughout diastole into auricular systole

IV   THE MURMURS OF HYPERTENSION

Patients in whom hypertension was associated with some other form of heart disease were excluded, and only those with hypertension alone were admitted for special study   A phono-cardiogram was recorded in 43 cases   in 16 it was used to tell the position of the added sound

that was initiating triple rhythm, in 14 to examine the auricular and ventricular moieties of the first heart sound which showed splitting on auscultation, in the remaining 13 to examine a systolic murmur in the mitral area that was a noticeable auscultatory sign

The Systolic Murmur

Routine clinical and radiological examination failed to explain with certainty what determined the presence of a systolic murmur in hypertension   The murmur did not disallow a triple heart rhythm because they were sometimes found together in the same patient   The murmur was not a product of associated aortic valvular disease, although in a group of patients, not included in this paper, where aortic incompetence accompanied hypertension, the mitral area was never without a systolic murmur   In hypertensive heart failure a mitral systolic murmur was common although certainly not invariable, but it was noticed that all patients with this murmur showed considerable enlargement of the heart   Thus, among the factors contributing to an apical systolic murmur in hypertension, cardiac enlargement was the most obvious   Further, when a number of patients with a systolic murmur and hypertension, but with only a moderate degree of cardiac enlargement, were examined by the phonocardiograph, mitral stenosis was found to be present although the signs of this had been inconclusive on clinical and radiological examination

On auscultation the murmur was always distinct, and often it was loud   It never disappeared on deep inspiration, and posture had little effect on it except that often it was heard best in the reclining posture   Being loud the murmur was heard some distance away from the seat of its maximum intensity in the mitral area   There was no selective direction for its propagation, and it was never directed specially towards the aortic area   A regard of the physical qualities of the murmur could not tell it from the systolic murmur of mitral disease, although the absence of a thrill justified the suspicion that it belonged to hypertension, especially if enlargement of the heart was considerable   Radiological examination most times could exclude the presence of added mitral disease and yet a prominent left auricular impression in the barium swallow in the right oblique position often called for care in interpretation   A low and distinctive curve in the left oblique position supported a diagnosis simply of hypertension where a normal left auricle had been displaced backwards by the enlarged left ventricle

In each of the 13 cases of hypertension with an apical systolic murmur, the phonocardiogram showed the murmur starting in mid-systole, a little way beyond the S line (Fig 28)
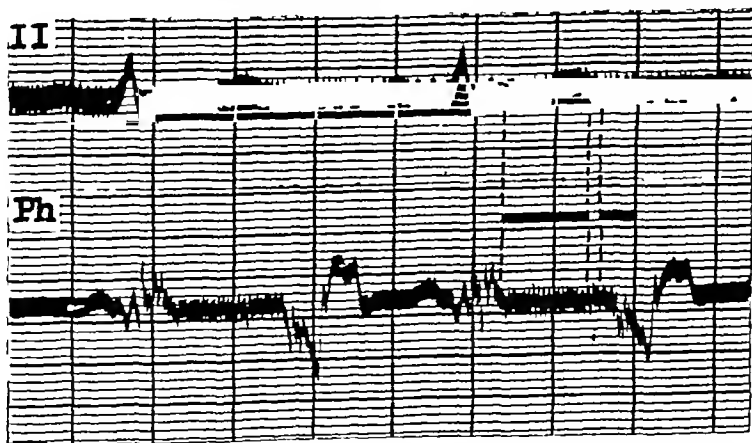
Fig 28 —Hypertension   The systolic murmur starts in mid-systole a little beyond the S line   A diastolic murmur accompanying the second sound continues in this case up to a prominent third heart sound

It sometimes lasted up to the second heart sound although occasionally the murmur had spent itself before the end of systole   This was in sharp contrast with the murmur of mitral disease which never once started later than the S line and generally started in front of it and during the P–R period of the electrocardiogram, that is, during auricular systole   Apart from the mid-systolic position of the murmur, the phonocardiogram of hypertension differed from that of the tracing of mitral valvular disease in that there was no mid-diastolic murmur   In the presence of *auricular fibrillation* the same features distinguished the phonocardiogram of mitral disease from that of hypertension, so that in hypertension the systolic murmur started in mid-systole and some way after the S line and there was no mid-diastolic murmur (Fig 20) whereas the systolic murmur in fibrillation from mitral stenosis started at the S line and a mid-diastolic murmur followed the third heart sound (Fig 29)   The start of the systolic murmur of hypertension in mid-systole also distinguished it from cases of aortic valvular disease where the murmur in most instances started at the S line

FIG 29 —Mitral stenosis and auricular fibrillation   The systolic murmur starts at the S line and a diastolic murmur follows the third heart sound

THE DIASTOLIC MURMUR

Among 43 cases of hypertension there were 12 whose phonocardiogram showed an early diastolic murmur (Fig 30), although in none could this murmur be elicited by auscultation The significance of these vibrations of high frequency (as with a murmur) following and contiguous with the second heart sound in the phonocardiogram has been examined, and the
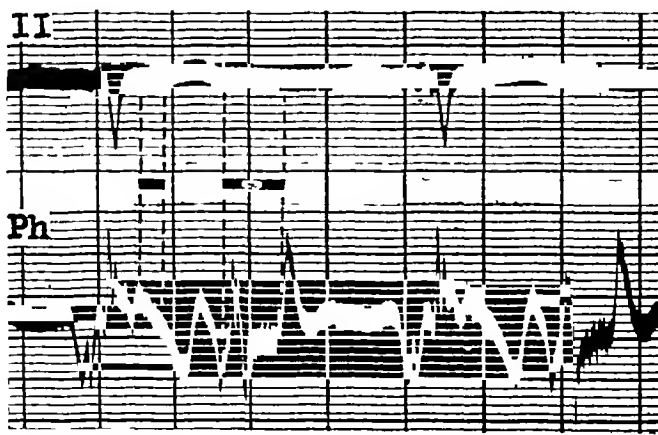
FIG 30 —Hypertension   A diastolic murmur, which was not heard clinically, accompanies the second heart sound

possibility considered whether the cause lies with the sudden distension of the aorta in hypertension during early diastole and not with the presence of relative aortic incompetence   In support of a degree of aortic reflux being present were the facts that such a sign was often absent from the sound tracing in cases where the diastolic blood pressure was high and in others where the second aortic sound was very loud, and the presence of the same murmur (or its phonocardiographic pattern) in aortic stenosis where the second sound was not loud and where the diastolic blood pressure was not raised

A diagnosis of *mitral incompetence* has been applied when a mitral systolic murmur is prominent among the physical signs of hypertension   In 13 patients with hypertension who showed a mitral systolic murmur, it never once coincided with the start of ventricular systole so that it was not produced by incompetence of the mitral valve

SUMMARY   MURMURS OF HYPERTENSION

The commonest murmur in hypertension is an apical systolic murmur   Cardiac enlargement above all else contributes to its appearance   Should a patient with a raised blood pressure, therefore, show a systolic murmur in the absence of more than moderate left ventricular enlargement, it is likely that the murmur arises from a source other than hypertension   The murmur starts in mid-systole and later than the S line in the phonocardiogram so that its mechanism is not mitral incompetence   An early diastolic murmur from relative aortic incompetence was often recorded in the sound tracing although it could not be heard but this graphic finding seems to be of secondary importance

V   THE MURMURS OF CONGENITAL HEART DISEASE

In this variety of murmurs too, phonocardiography has proved useful in confirming a diagnosis when there was doubt and in excluding the innocent kind   The conditions in which the phonocardiogram was most used were patent ductus arteriosus, pulmonary stenosis auricular septal defect, ventricular septal defect and coarctation of the aorta

PATENT DUCTUS ARTERIOSUS

A sound record was taken in 11 cases of undoubted patent ductus arteriosus and a distinctive murmur was found in each   Clinically the murmur was loud and of the machinery kind and was accompanied by a thrill   The third heart sound was never identified on
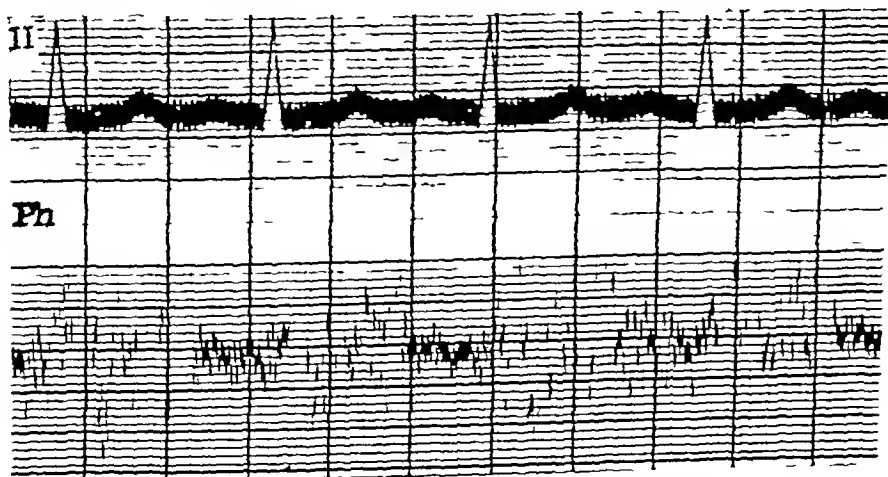
FIG 31 —Patent ductus arteriosus   The murmur starts at the S line and soon increases but it declines in mid-systole to increase again in late systole and reaches its height at the second heart sound which it embraces   it also obscures the third heart sound and occupies the rest of diastole as a moderate murmur
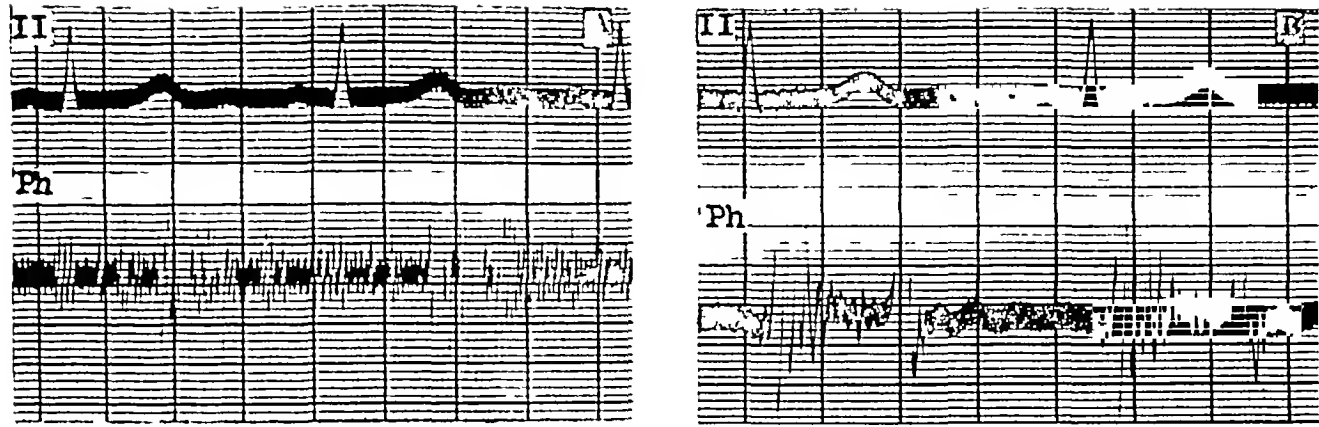
Fig 32 —Patent ductus arteriosus   The characteristic continuous murmur present in (A) is absent in (B) which was recorded after the duct was ligated

auscultation amongst the murmurs   Phonocardiographically the murmur was found to be as distinctive as it was clinically, its main characteristic being its continuity throughout systole and diastole   Indeed, when tracing this murmur the galvanometer string is never still (Fig 31 and 32)   The murmur in early ventricular systole starts at the S line, and a little later it becomes more obvious, in mid-systole the murmur wanes, in late systole the murmur increases in intensity at a point corresponding with the summit of the T wave in the electrocardiogram, and at the end of the T wave, where the second heart sound occurs, the murmur is at its height   After thus embracing the second sound it declines until it reaches the position of the third heart sound which it also obscures   Thereafter it continues as a subdued murmur throughout the remainder of diastole and auricular systole   This graphic finding explains the difficulty met with in some cases of patent ductus arteriosus of discovering the second heart sound within the murmur during auscultation

PULMONARY STENOSIS

A phonocardiogram was recorded in 14 cases, in 11 of these the pulmonary stenosis was considered to be a lone lesion, while in the remaining 3 there was also present a defect of the ventricular septum (Fallot s syndrome)   In the first group the murmur in the pulmonary area was loud, and sometimes harsh, and was accompanied by a thrill   In the second group it was less loud and a thrill was absent twice   In both groups the murmur, although louder in the reclining posture, was easily heard in the upright posture   The second heart sound was present as a rule, and no diastolic murmur was heard in these patients

The murmur in early ventricular systole commenced at the S line, in mid-systole the murmur waned, in late systole it usually increased in intensity at a point coinciding with the beginning of the T wave of the electrocardiogram, until it reached the second heart sound which it embraced, but it ceased before the third heart sound was reached   The relative intensity of the murmur in early and late systole varied so that sometimes it was louder in early systole (Fig 33), and at other times it was louder in late systole (Fig 34)

THE INNOCENT PULMONARY SYSTOLIC MURMUR

A systolic murmur in the pulmonary area is a common finding in young subjects, and since so little has been spoken about the differentiation of the innocent murmur from that of pulmonary stenosis, it is a common cause of unwarranted invalidism   Phonocardiography has contributed materially in differential diagnosis because it has confirmed the validity of the clinical signs that identify this innocent murmur
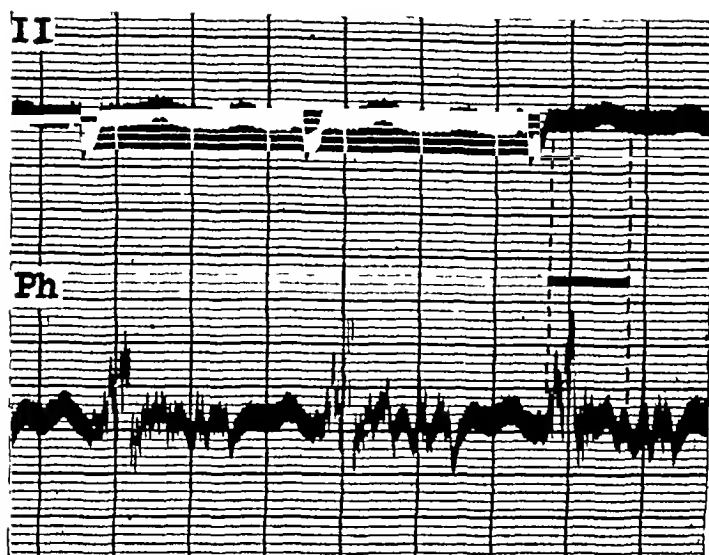
FIG 33 —Pulmonary stenosis   The systolic murmur starting at
the S line is more intense in early ventricular systole, it em-
braces the second sound, but it is spent before reaching the
third heart sound
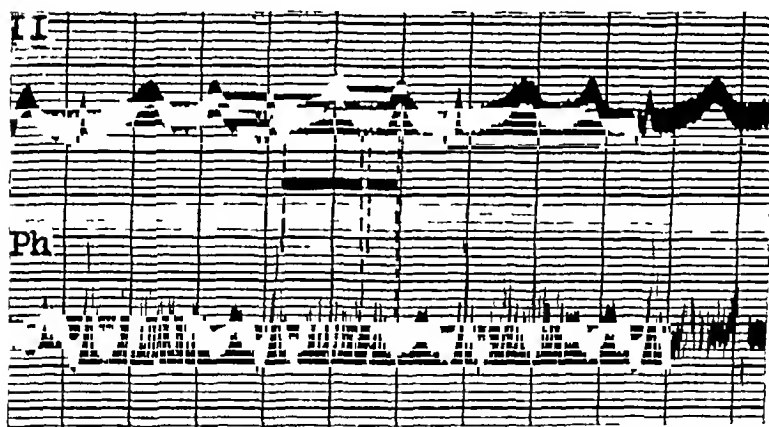
FIG 34 —Pulmonary stenosis   The systolic murmur which starts at the
S line is more intense in late ventricular systole, it overlaps the
second sound but disappears before the third heart sound

The murmur was rough in quality and sometimes it was moderately loud   The effect of
posture was a valuable test, for the murmur was much less noticeable in the upright posture,
especially when combined with deep inspiration   This innocent murmur was never accom-
panied by a thrill although the absence of this sign could not be accepted as evidence of the
innocence of the murmur since it was often absent when pulmonary stenosis was associated
with ventricular septal defect   These clinical signs could not be controlled by reference to
the electrocardiogram nor to cardioscopy in both of which negative findings at such tests
did not mean that pulmonary stenosis could be excluded, although positive findings were
naturally evidence of the organic lesion
    The phonocardiogram will prove a valuable aid to the diagnosis, and in the mean-
time it has supported the physical signs that have been regarded as the basis of a clinical
judgment on the innocence or otherwise of the common systolic murmur in the pulmonary
area   The distinctive feature of the sound record was that the murmur started in mid-systole

a little later than the S line and had largely spent itself before reaching the second heart sound (Fig 35), naturally there were no diastolic murmurs present

FIG 35—The innocent murmur in the pulmonary area The murmur starts in mid-systole and it has spent itself before reaching the second heart sound

AURICULAR SEPTAL DEFECT

When a cardiological examination includes an electrocardiogram and cardioscopy, this congenital defect will seldom be missed because of the characteristic signs that these will show Clinically, however, its recognition continues to remain uncertain The pulse is usually small, the apex beat is out, and a systolic murmur is seldom absent along a line from the base to the apex, but greatest reliance is placed on finding an early diastolic murmur in the pulmonary and mitral areas which is probably not heard to the right of the mid-line as is the murmur of aortic incompetence When such a murmur is present—and it has a high incidence—moderate or greater dilatation of the pulmonary artery can be predicted on radiological examination for it is the outcome of relative pulmonary incompetence from dilatation of the arterial ring If a clear third heart sound is heard along with this murmur the diagnosis of auricular septal defect is more certain

The auscultatory findings are shown characteristically in the phonocardiogram (Fig 36) with the systolic murmur starting at the S line, the early diastolic murmur following immediately after the second heart sound, and a clear third heart sound beyond This phonocardiographic finding is in contrast with the early diastolic murmur of rheumatic aortic incompetence when the third heart sound, if present, is often followed by the mid-diastolic murmur of mitral
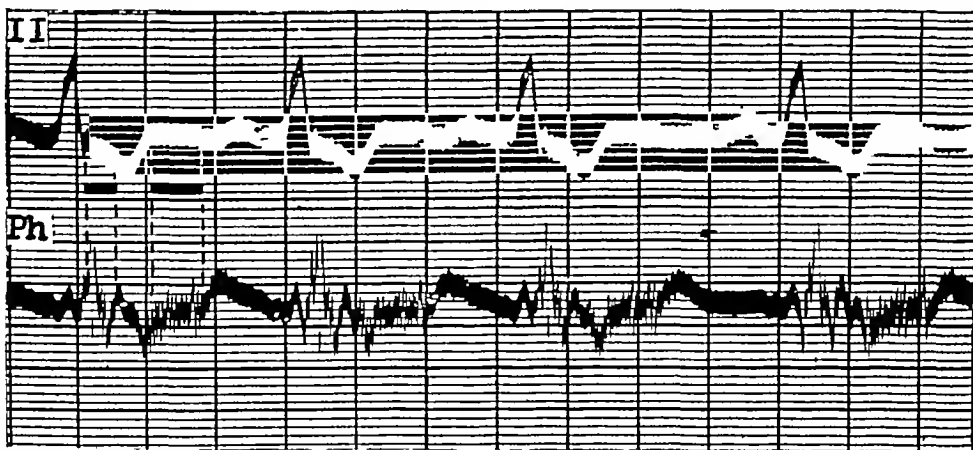
FIG 36—Auricular septal defect The systolic murmur starts at the S line and the diastolic murmur of pulmonary incompetence accompanies the second heart sound and lasts as far as the prominent third heart sound

In the second circumstance, the phonocardiogram shows the murmur commencing in mid-systole, but if it arises in the hypertrophied arteries it is even later in systole (Fig 38) The incidence of relative aortic incompetence, producing an early diastolic murmur in the sound record, is commoner in coarctation hypertension than in other forms of hypertension

SUMMARY MURMURS OF CONGENITAL HEART DISEASE

The murmur of *patent ductus arteriosus* is a continuous one lasting throughout systole and diastole, with intensification in early diastole where it covers the second heart sound and proceeds to obscure the third heart sound as well

The murmur of *pulmonary stenosis* starts at the S line and lasts till it reaches the second heart sound which it embraces, but it ends before reaching the third heart sound   The murmur appears earlier in systole than the innocent pulmonary murmur, commencing as it does at the S line of the phonocardiogram

An early diastolic murmur from pulmonary incompetence followed by the third heart sound are the characteristic phonocardiographic findings in *auricular septal defect*   When mitral stenosis is added to the congenital anomaly (Lutembacher's syndrome) there are added auricular and mid-diastolic murmurs

The systolic murmur of *ventricular septal defect* commences at the S line and thus differs from the innocent parasternal murmur which starts in mid-systole, it also lasts longer

The common systolic murmur in *coarctation* is the one heard over the hypertrophied arteries of the collateral circulation so that it occurs late in systole   Less frequently the murmur comes from the greatly enlarged heart and aortic incompetence is then usually present, so that the murmur is earlier in systole

VI   THE MURMUR OF HEART BLOCK

A systolic murmur in the mitral area in heart block is only found when the heart is greatly enlarged   It is a rough murmur and it may be loud   Posture is without much effect on its intensity although it is sometimes better heard when the subject inclines to the left   A thrill is never present unless there is mitral or aortic valvular disease as well

In seven cases of complete heart block with a systolic murmur in the mitral area, the phonocardiogram showed the murmur starting in mid-systole (Fig 39)   Graphically it was
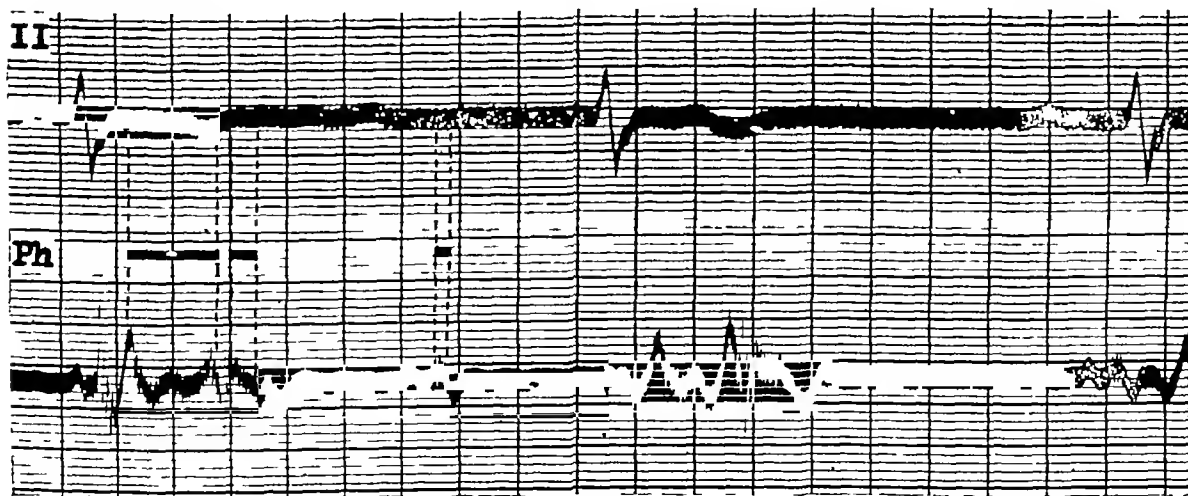
FIG 39 —Complete heart block   The systolic murmur starts in mid-systole, and a diastolic murmur follows the second heart sound   The murmurs are similar to those found in hypertension associated with much cardiac enlargement   The natural auricular diastolic murmur is also recorded

similar to the murmur of hypertension except that the tracing did not as often show an early diastolic murmur which was sometimes present in the record from a case of hypertension Although hypertension appeared along with complete heart block in three cases, the systolic murmur was in the same situation in the other four without hypertension

SUMMARY MURMURS OF HEART BLOCK

The systolic murmur of complete heart block has been shown by the phonocardiogram to start in mid-systole Thus, the mechanism of the murmur in heart block as well as of the one in hypertension appears to be connected with the muscular contraction of a much enlarged heart, the start in mid-systole excludes a valvular origin for the murmur

VII THE MURMUR OF ANÆMIA

Although an obvious murmur is heard in the majority of patients with a significant anæmia, it is sometimes absent even when the anæmia is severe Its presence does not depend on the size of the heart The murmur as a rule is widely distributed and may be heard in the aortic area as well as in the pulmonary and mitral areas, when present in more than one area it is usually loudest in the pulmonary The murmur varies in intensity so that it may sound faint or rough, and it is better heard in the reclining than the upright posture Although diastolic murmurs have been described in anæmia, I have never heard them
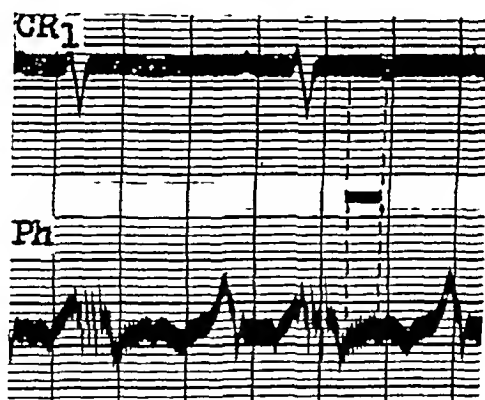
FIG 40 —Anæmia The systolic murmur starts in mid-systole some way after the S line A prominent third heart sound follows the second

Whenever the phonocardiogram was recorded it showed the murmur starting in mid-systole (Fig 40) An obvious third heart sound was seen whenever the heart was enlarged as the result of the anæmia

SUMMARY MURMURS OF ANÆMIA

The only murmur to show in the phonocardiogram from patients with anæmia was the one in mid-systole A diastolic murmur was not once recorded

GENERAL SUMMARY AND CONCLUSIONS

The heart murmurs in 500 healthy subjects and patients with heart disease were specially examined, both by clinical auscultation and by phonocardiography The object of the investigation was to determine the physical characteristics of murmurs that would make their clinical recognition both easier and more certain Ancillary methods of examination including electrocardiography were used whenever necessary, and cardioscopy was never omitted Necropsy was sometimes available

Foremost amongst the findings of the investigation was the clinical identification of the *innocent mitral systolic murmurs* which continue to cause widespread unwarranted invalidism because of their common appearance, on this account their recognition is a matter of concern unequalled by any other in clinical cardiology   The situation and distribution of these murmurs and the effects upon them of a change in posture and deep breathing make it possible to tell them from the murmurs of organic heart disease   The phonocardiograph confirmed this clinical classification and located the murmurs either in mid-systole or late systole, it also showed the absence in such cases of auricular systolic and diastolic murmurs   In patients with *mitral stenosis* the phonocardiograph showed that the murmur which presented clinically as a systolic murmur usually started during the P–R period of the electrocardiogram, that is during auricular systole, as did the presystolic murmur   Even in the few exceptions where the murmur was later and coincided with the start of ventricular systole, the term " mitral incompetence " would have been incomplete as in each there was a mid-diastolic murmur giving proof of mitral stenosis   The common incidence of a mid-diastolic murmur immediately succeeding the third heart sound in mitral disease, for it was found in each of 74 cases, stimulates the clinical search for this murmur in patients suspected of the condition   Should future investigation show that this is an invariable graphic finding in mitral disease it will prove to be a physical sign of inestimable value

In *aortic valvular disease* the systolic murmur, which was an unfailing sign in the mitral area, was seen phonocardiographically to start synchronously with the start or early part of ventricular systole   The test showed the common incidence in aortic stenosis of the early diastolic murmur of aortic incompetence although this sign had not yielded to clinical auscultation   The phonocardiograph has often demonstrated an early diastolic murmur when aortic incompetence is unsuspected by casual or even careful clinical examination   On this account too the test has proved of great value

The mitral systolic murmur in *hypertension*, making its appearance whenever the heart is greatly enlarged, was recorded in mid-systole and a little time after the ventricle had commenced to contract, such a finding opposes the assumption that this murmur is the outcome of mitral incompetence   Doubtless it is the result of muscular contraction and the same murmur was found when the heart was much enlarged in *complete heart block*   In both conditions an early diastolic murmur of relative aortic incompetence, resulting from dilatation of the aortic ring, was a fairly common event, and when it was present it served to emphasize the presence of considerable left ventricular enlargement

The phonocardiogram in *congenital heart disease* helped to tell the innocent parasternal murmur from that of ventricular septal defect, and the innocent pulmonary systolic murmur from that of pulmonary stenosis   The test demonstrated the continuity of the murmur of patent ductus arteriosus with its accentuation in early diastole   An early diastolic murmur from pulmonary incompetence, leading up to an obvious third heart sound, was never absent in the sound tracing from cases of auricular septal defect, when mitral stenosis was added to the congenital lesion (Lutembacher's syndrome) so were auricular systolic and mid-diastolic murmurs to the phonocardiogram   The murmur of coarctation of the aorta was written in late systole   In *anæmia* the murmur started in mid-systole and a diastolic murmur was not once recorded

This phonocardiographic study of heart murmurs has shown that the quality and intensity of murmurs matter far less than their place in the cardiac cycle and in relation to the heart sounds   Such a finding emphasizes the need for self-catechism during clinical auscultation when precise answers should be sought to six set questions   The questions concern the character of the first heart sound and similarly of the second heart sound, the presence of more than two sounds, and the presence of murmurs connected with the first heart sound

(presystolic and systolic), with the second heart sound (late systolic and early diastolic), and with the third heart sound (mid-diastolic) When such simple auscultatory procedure has become custom, cardiological diagnosis will have gained immeasurably in accuracy

REPETITIVE PAROXYSMAL TACHYCARDIA

BY

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Paroxysmal tachycardia might be defined as sudden attacks of extreme acceleration of the heart that last from a few seconds to a few days and end abruptly as they begin   In the average patient with paroxysmal tachycardia the paroxysm is the exception   normal rhythm is the rule, the difficulty is to obtain an electrocardiogram during the attack   We have become interested in a special variety where recurrent paroxysms are the rule and normal rhythm is the exception, the difficulty now is to obtain the normal electrocardiogram   This variety is here described as *repetitive*   It is characterized by recurring short runs of auricular, nodal, or ventricular extrasystoles, runs or paroxysms of tachycardia in fact, almost constantly present for months or for years and only occasionally interrupted by the normal sinus rhythm   We do not include under this term the recurrent brief paroxysms of tachycardia which may happen to be portrayed on an isolated electrocardiogram   It is true that in a sense they are repetitive, but this is an incident, not a clinical state like that of repetitive paroxysmal tachycardia where the play of paroxysms almost displaces normal rhythm   Its separate consideration is justified on clinical grounds, for it more often affects children and young people in whom it presents a novel problem in prognosis   There are few conditions in children of which it can be said that they are likely to " grow out of it," but this appears to be one

It is 20 years since one of us (J P) came across our Case 1, and since then we have records, more or less complete, of 40 cases of repetitive paroxysmal tachycardia   Cases to be quoted below have been reported singly or perhaps in twos or threes   Our plan was to place on record for the first time a large group of such cases   We have since found, however, in the monograph of Léon Gallavardin (1946), a study of this nature under the title " Extrasystolie auriculaire en salves," differing from ours in that it relates to auricular paroxysms only

Lewis (1909) made the first observation of this kind in a man of 41 with an otherwise healthy heart   By continuous polygraphic record during 109 minutes he was able to count 54 short paroxysms of auricular paroxysmal tachycardia at a rate of 133–184   Paroxysms of over 1 minute duration were rare, the shortest attack consisted of a succession of a few ectopic beats, the longest lasted 7 minutes   Though occurring at rest, they were more frequent on exertion   Even at a slow rate the pulse was hardly ever regular because of single or multiple auricular extrasystoles

White (1920) drew attention to the " markedly rapid but not immediate " increase in rate and similar offset during the short and continuously recurring attacks of auricular paroxysmal tachycardia in his patient observed for five years   Scott (1922) abolished with quinidine the short and continuously recurring attacks of ventricular tachycardia which were precipitated by exertion and were the cause of serious invalidism in this patient

Louis Gallavardin (1922, *a*, *b*, and *c*) insisted on their distinction from ordinary paroxysmal tachycardia and described the ventricular variety in one case (Gallavardin, 1922*b*) and the auricular variety in three others (Gallavardin, 1922*c*), under the name of " Extrasystolie

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a paroxysmes tachycardiques " Later with Dumas (Gallavardin and Dumas, 1924) he used the name of " tachycardie en salves " in adding three more supraventricular cases He also noticed in some that effort produced the paroxysms (Gallavardin, 1922a) and that the ventricular form frequently caused attacks of giddiness comparable with those in Stokes-Adams disease Later with Veil (Gallavardin and Veil, 1929a and b) he added four similar cases which also include the one already published in 1922, after 15 years of observation the patient was still having the short and continuously recurring paroxysms of ventricular tachycardia

Cassidy (1924) recorded an " incessant " paroxysmal tachycardia in an otherwise healthy child of 8, who had short bursts of auricular paroxysmal tachycardia every few minutes, constantly recurring during two years of observation

In Gilchrist's (1925–6) Case 5 with ventricular tachycardia mostly on exertion " an intimate mixing of short ventricular paroxysms, multiple and isolated ventricular extrasystoles and occasional sinus beats " were continuously recorded for six months until they were abolished with quinidine

Wenckebach and Winterberg (1927) reported two instances of almost continuous auricular paroxysmal tachycardia with varying A-V block, watched for two and three months respectively In three other cases short bursts of ventricular paroxysmal tachycardia were constantly found, and in two of these effort produced longer attacks They conclude that it would be better to distinguish a persistent form of paroxysmal tachycardia from the usual one occurring in attacks, as one does in flutter

Single cases of the ventricular variety were described by Jones and White (1926–7), Schliephake and Graubner (1928), Lutembacher (1929), Andersen (1931), and Berard (1931) In Gallavardin and Froment's (1930) case salvos of ventricular tachycardia co-existed with auricular paroxysmal tachycardia of the classical type In McMillan and Bellet's (1931–2) patient, also with the ventricular form, a Cæsarean section was successfully performed while she was in the state of paroxysms Wilson and others (1932) in adding four similar cases insist on the absence of structural heart disease, the relation of the paroxysms to exertion, their brevity, and the effectiveness of quinidine This was also successfully employed in other ventricular cases quoted above

Froment (1932) dedicates part of his admirable monograph on ventricular paroxysmal tachycardia to the " Extrasystolie ventriculaire bénignes á paroxysmes tachycardiques " He draws a sharp distinction between these and the " grave," " terminal," or " prefibrillatory " ventricular tachycardias and insists that the denomination of ventricular paroxysmal tachycardia should be reserved for these only while the former benign condition should be called extrasystolia Transitional forms, however, are described where prolonged observation was necessary before placing the case into the one or the other group Diagnostic criteria are given in favour of " extrasystolia," namely, the uniform shape of the extrasystolic complexes forming the tachycardiac runs, the normality of the intervening sinus beats, the youth of the patient, the integrity of the cardiovascular system, and the long evolution of the arrhythmia Twenty cases are reported from the literature and no original cases are added

The prognosis in general has been reported good An exception was the 56-year-old patient of Clerc et al (1933) with habitual ventricular tachycardia who died suddenly Then, Elliott and Fenn (1934) described a 29-year-old woman in whom ventricular paroxysmal tachycardia with shorter or longer intermissions lasted for more than three months, after which she died of congestive heart failure Each of these patients had an enlarged heart and an abnormal cardiogram between the attacks Maddox (1947) has added a case in which there was a sudden mortal termination Routier and Puddu (1936) and Routier (1937), describing three cases of benign ventricular extrasystoles in the form of paroxysmal tachycardia, also stress the good prognosis, provided there is no cardiac enlargement and the cardiogram is normal between the attacks Campbell and Elliott (1939) also believe that the type " of very short

paroxysms recurring frequently, may be found with a normal heart and seems to be of no serious significance, even though it is ventricular "

Fine and Miller (1940) describe an " orthostatic " auricular paroxysmal tachycardia observed for two years, in whom the attack could be produced at will by change of posture, though it was also found sometimes at rest and in the supine position   Four years later the patient, who had congenital lues, died suddenly during malaria therapy (Miller and Perelman, 1945)   On the other hand a similar patient, a healthy girl of 14, with " chronic auricular tachycardia " at rest and especially on change of posture, was able to live an active life during three years of observation (Miller and Perelman, 1945)   Peters and Penner (1946) describe an orthostatic paroxysmal ventricular tachycardia successfully treated with quinidine   Graybiel and White (1946), in commenting on a cardiogram of recurrent auricular paroxysmal tachycardia, find it decidedly uncommon and believe that it is " in itself no evidence of heart disease "

Leon Gallavardin (1946) in an exhaustive study of the auricular extrasystole has collected 31 cases of " extrasystolie auriculaire en salves," partly original, partly previously published by his father (Louis Gallavardin) and others, with observation periods ranging from a few months to 29 years   In two-thirds of the cases the arrhythmia was the only cardiac abnormality while in the remaining one-third heart disease was present   He insists on distinguishing the arrhythmia characterized by the short and continuously recurring attacks from ordinary paroxysmal tachycardia, and gives a complete description of its clinical and electrocardiographic peculiarities

In addition to these references mostly describing repetitive paroxysmal tachycardia separately, a number of examples are included in papers dealing with paroxysmal tachycardia in general   Williams and Ellis (1943) in analysing 36 cases of ventricular tachycardia found 12 belonging to the " intermittent " type   This group which included their only patient with no organic heart disease carried a less serious prognosis than the other group with persistent ventricular tachycardia   In Cooke and White's (1943) list of 32 cases of ventricular paroxysmal tachycardia, Cases 24, 25, and 27, and Freundlich's (1946) Case 3, probably belong to this variety, and so do several of Barker, Wilson, and Wishart's (1943) cases, their Case 1 is our Case 12, and Campbell's (1945) Case 2 is our Case 2

The various names under which this kind of paroxysmal tachycardia has been described indicate the uncertainty hitherto felt on the subject   While some hold that the relation to exertion or posture is the most characteristic feature, others stress the " incessant," " chronic," or " habitual " nature of the paroxysms   The name " repetitive " seems to us to express best the very frequent recurrence of the paroxysms

BASIS OF INVESTIGATION

The following account is drawn from a series of 40 patients with repetitive paroxysmal tachycardia   Most of these were seen personally at the Cardiac Department of the London Hospital or at the National Heart Hospital, some were seen privately and others are added through the courtesy of friends   Sometimes the unusual character of the pulse, sometimes the routine cardiogram itself, led to the recognition of this variety of paroxysmal tachycardia   Apart from clinical and electrocardiographic examination, observations were frequent to obtain confirmation of its repetitive nature   The war has made a follow-up more difficult, but some have responded (see Tables)

CLINICAL FEATURES

Ages extended from the youngest aged 4 years to the oldest aged 75   The auricular form is common in those under 40 and particularly so in children   Flutter and fibrillation in this form are commoner in the adult than in the young, as would be expected   The sex incidence is males   females about 2   1

Observations ranging from 18 years to 3 months was possible in more than half the cases (see case notes and Tables)   The longest the paroxysmal state persisted was 10 years   Eleven patients were seen once or twice only   The diagnosis was here based on medical reports of almost incessant tachycardia or arrhythmia, on their long-standing symptoms, and of course on the characteristic electrocardiogram

Symptoms and clinical features were similar in all groups irrespective of the electrocardiographic pattern   The common symptom was palpitation, usually continuous and independent of exertion, a few complained of slight breathlessness in addition   Six had syncopal attacks, which in three (all ventricular) constituted the main feature (Cases 32, 33, and 39)   Unfortunately we never had an opportunity of observing the patient when they occurred   In the absence of evidence of heart-block at any time, we do not regard them as examples of Stokes-Adams attacks (Parkinson, Papp, and Evans, 1941)   Symptoms were often present over many years (Table I), and were severe enough in seven (Cases 3, 7, 12, 15, 19, 32, 39) to restrict

TABLE I

CASES OF REPETITIVE AURICULAR PAROXYSMAL TACHYCARDIA

Case No Sex, and Age	Duration of symptoms when first seen	Under observation	Repetitive paroxysms observed	Follow-up
1 M 6	1 month	18 years	10 years	Well, no paroxysms
2 M 7	—	6 years	5 years	—
3 F 22	5 years	6 years	6 years	—
4 M 20	2 years	5 years	5 years	—
5 M 11	—	7½ years	3 years	Still paroxysms
6 F 30	—	3½ years	7 months	—
7 M 25	2 years	2 years	2 years	—
8 M 11	—	2½ years	2½ years	—
9 M 46	—	2½ years	2½ years	Still paroxysms
10 M 6	2 years	9 months	9 months	Still paroxysms
11 F 11	—	3 months	3 months	Well after 4 yrs No paroxysms
12 M 39	9 years	5 years	6 months	—
13 M 9	5 years	—	? 9 years	Well after 13 yrs No paroxysms
14 M 59	10 years	4 years	4 years	Still paroxysms
15 F 50	20 years	8 months	8 months	Still paroxysms
16 F 23	14 months	10 months	3 months	Well, no paroxysms
17 M 35	—	5 years	5 years	Still paroxysms
18 M 18	—	4 years	4 years	Still paroxysms
19 F 20	—	3 years	3 years	—
20 M 18	—	1 year	1 year	Still paroxysms
21 M 18	—	6 months	1 month	Well, no paroxysms
22 M 19	—	4 years	2 months	Well, ? paroxysms
23 M 39	—	Seen once	—	—
24 M 37	3 weeks	Seen once	—	—

TABLE II

CASES OF REPETITIVE FLUTTER (CASES 25–28) AND OF AURICULAR FIBRILLATION (CASE 29)

Case No Sex, and Age	Duration of symptoms when first seen	Under observation	Repetitive paroxysms observed	Follow-up
25 F 34	months	3 years	3 years	—
26 M 55	—	Seen once	—	—
27 M 52	months	Seen once	—	Well after 16 yrs ? paroxysms
28 M 75	5 years	Seen once	—	—
29 M 56	2 years	Seen once	—	Failure after 4 years

TABLE III

CASES OF REPETITIVE NODAL PAROXYSMAL TACHYCARDIA

Case No , Sex, and Age	Duration of symptoms when first seen	Under observation	Repetitive paroxysms observed	Follow-up
30 F 22	3 months	2 years	2 years	Less palpitation
31 F 56	13 years	3¼ years	3¼ years	—

TABLE IV

CASES OF REPETITIVE VENTRICULAR PAROXYSMAL TACHYCARDIA

Case No , Sex, and Age	Duration of symptoms when first seen	Under observation	Repetitive paroxysms observed	Follow-up
32 F 35	1 year	13 years	2¼ years	Well after 12 yrs No paroxysms
33 M 20	4 years	1 year	1 year	Still paroxysms
34 F 4	2 months	11 months	11 months	Still paroxysms
35 M 36	4 years	4 months	4 months	Well after 10 years No paroxysms
36 M 57	1 year	Seen once	—	Well after 4 yrs No paroxysms
37 M 57	12 years	Seen once (hypertension)	—	Died in failure after one yr
38 F 60	1 year	Seen twice	—	Well after 9 yrs No paroxysms
39 F 67	1 year	Seen twice	—	Well after 5 yrs No paroxysms
40 F 45	2 years	1¼ months	1¼ months	Still paroxysms

their physical activities   In the others the disability was minimal, though of six who were in the Services, three (Cases 4, 7, 33) had to be discharged   Seven children and seven adults were symptomless

It is a remarkable fact that evidence of organic heart disease was found only in three patients   Case 37 with the ventricular form had hypertension and cardiac enlargement, he died suddenly three years later in failure   Case 40, also with the ventricular form, had slight cardiac enlargement of obscure origin and inversion of T I   Case 8 with the auricular form had congenital heart disease (atrial septal defect)   Case 14 and Case 15, both with the auricular form, had toxic goitre, and Case 32, with the ventricular form for 5 years, had only single ventricular extrasystoles when six years later she was found to have a goitre

ELECTROCARDIOGRAPHIC FEATURES

The 40 cases were classified according to the electrocardiographic findings as follows
  (1) Repetitive auricular paroxysmal tachycardia, 24 cases
  (2) Repetitive flutter, 5 cases
  (3) Repetitive nodal paroxysmal tachycardia, 2 cases
  (4) Repetitive ventricular paroxysmal tachycardia, 9 cases
Repetitive auricular fibrillation might have formed another group, but it was seen only once and then only a single cardiogram was obtained   This case is included in Group 2

(1) REPETITIVE AURICULAR PAROXYSMAL TACHYCARDIA

In 16 patients—they include the six cases of latent and partial block—the same type of extrasystole always formed the runs whether short or long (Fig 1)   P was inverted in leads I and II in one case, in leads II and III in seven, and was upright in six, it was bifid in one case and diphasic in one   If upright, the P always differed in some respect from the normal P of the sinus beat
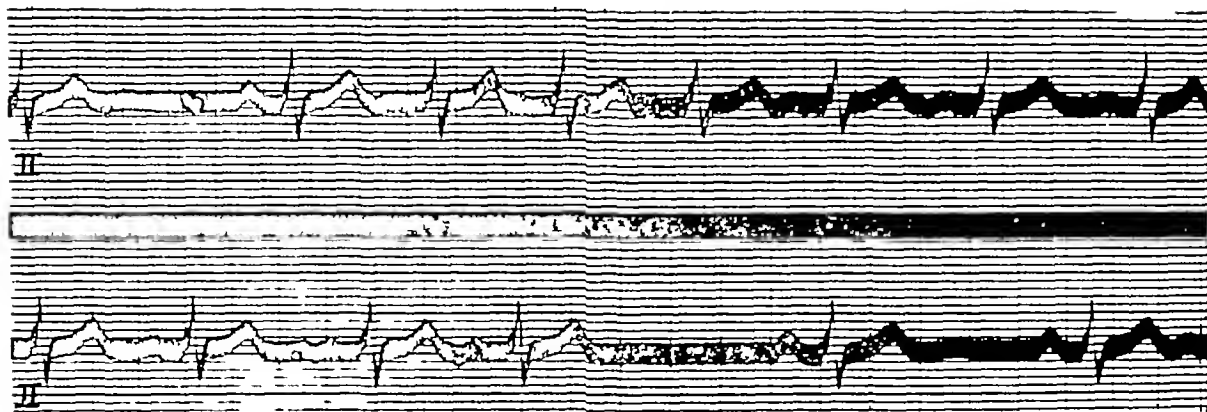
FIG 1 —Repetitive auricular paroxysmal tachycardia (R A P T)   Case 23   Beginning and end of paroxysm which is irregular, rate 90   Note change in P
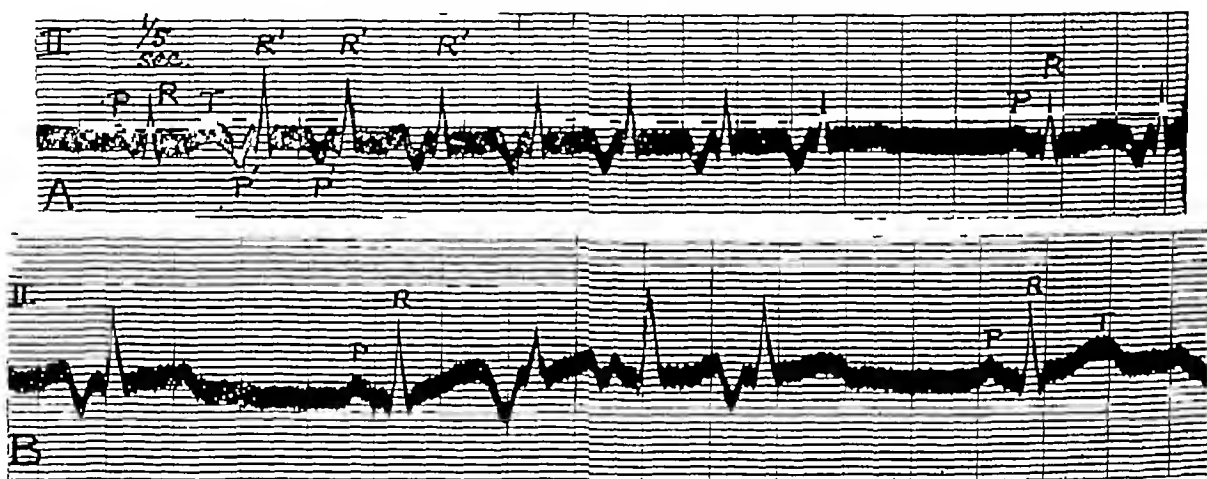
FIG 2 —R A P T   Case 1   (A) Run of auricular tachycardia, rate 170, regular   (B) Short run of multiform auricular extrasystoles at a similar rate, but irregular

In five patients, besides the recurrent short paroxysms like ordinary paroxysmal tachycardia as described above (Fig 2A), there were many other brief paroxysms of an extrasystolic type—apparently runs of multiform auricular extrasystoles, irregular and some with bizarre ventricular complexes (Fig 2B)

In two patients (Cases 7 and 14) these extrasystolic runs alone were recorded (Fig 3) In 4 out of 24 cases, blocked auricular extrasystoles added to the disorder of the rhythm (Fig 4) They were frequent during digitalis treatment   The rate in children was around 150   The rate in adults was noticeably lower, the highest was 150 in Case 3, the lowest 90 in Case 5, and on the average it was 120–130   The rhythm during paroxysms of paroxysmal tachycardia type was regular in 15, more or less irregular in 7 where the paroxysms were of a low rate (around 100) and of a short duration (3–7 beats) (Fig 1)   Even if regular, a slight slowing might occur towards the end of the paroxysm through a slowing of the last beats or through a slight prolongation of the P–R interval

Repetitive Auricular Paroxysmal Tachycardia with Block   During paroxysms latent block and higher grades of A-V block were found in 7 cases   The P–R interval during paroxysms was prolonged to 0 26 sec in Case 13,   Case 18 had Wenckebach periods (Fig 5A), and Case 9

FIG 3 —R A P T   Case 14   Run of multiform auricular extrasystoles, rate 145, very irregular, forming repetitive paroxysms
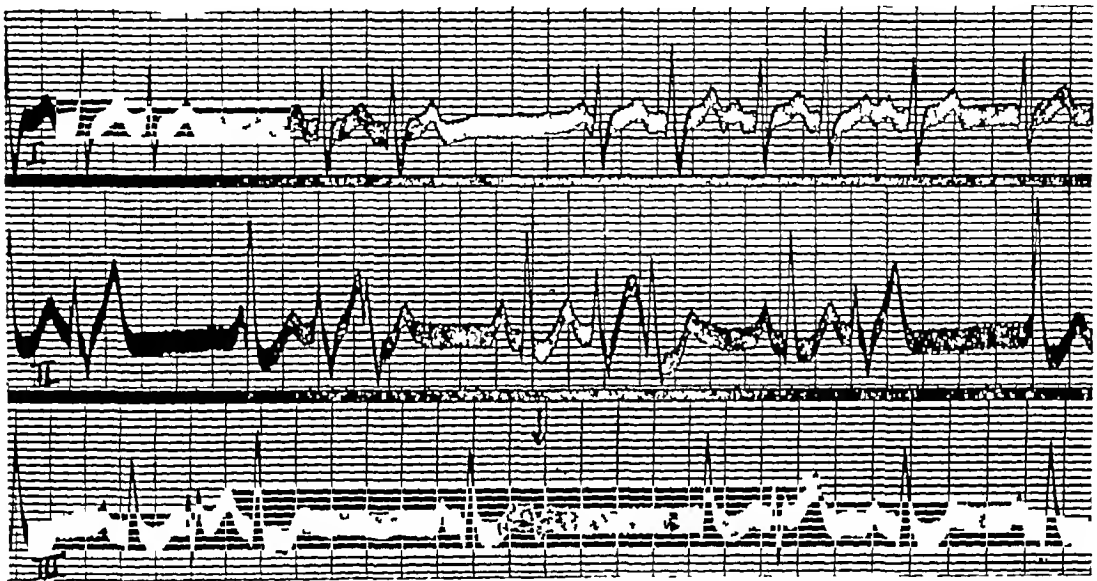
FIG 4 —R A P T   Case 6   Lead I   run of auricular paroxysmal tachycardia, rate 145, irregular
Lead II   groups of multiform auricular extrasystoles   Lead III   blocked auricular extrasystole
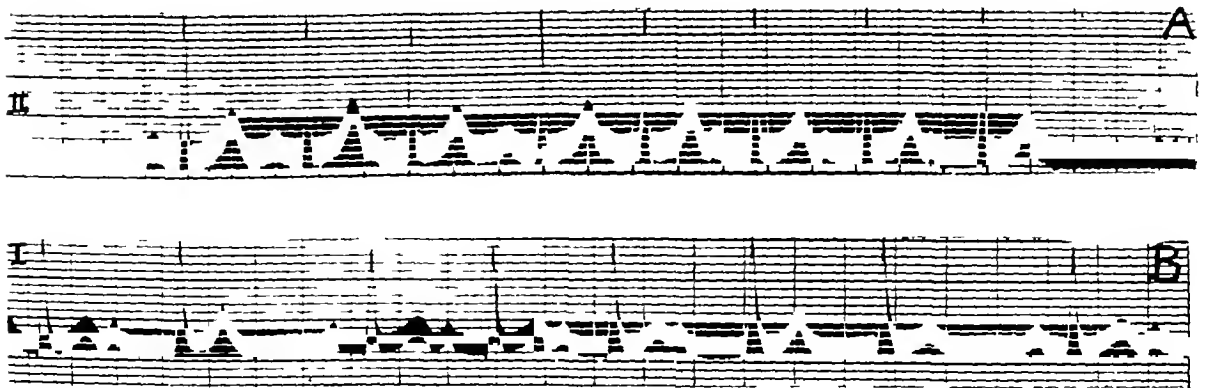
FIG 5 —R.A P T   with Wenckebach periods   (A) Case 18, prolongation of P–R interval at the end of paroxysm from 0 16 to 0 24 sec   (B) Case 9, progressive prolongation of P–R interval from 0 18 to 0 36 sec during paroxysm   Dropped beats in both cases, rate 120 slightly irregular

showed at times Wenckebach periods and at other times regular tachycardia at a rate of 130 with P–R 0 2 sec (Fig 5B)

Heart block was found in 4 cases   In Case 2, 2   1 A-V block developed as soon as the auricular rate rose to about 300, in Case 16 when about 200 (Fig 6)   In Case 12, block of
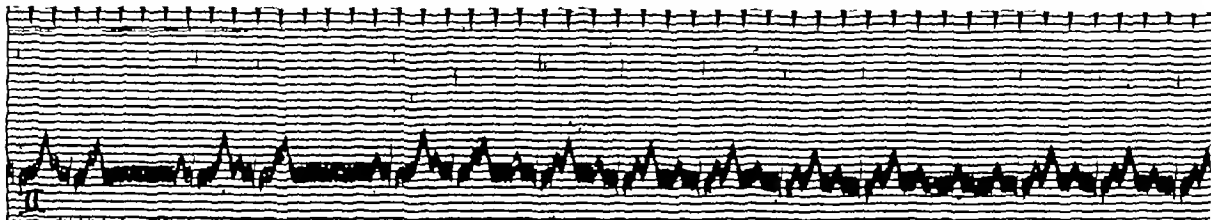
FIG 6 —R A P T with 2   1 A-V block   Case 16   Auricular rate 200, regular, ventricular rate half

2   1 and of higher degree might be present at a rate of 160–170, while at other times normal conduction was found at a rate of 200   In Case 8, 2   1 block was recorded all the time except when quinidine reduced the auricular rate from 180 to 105

Case 8 had congenital heart disease and he always had a prolonged P–R interval of 0 22, Case 2 when normal rhythm became re-established also had a P–R interval of 0 24 sec and a right bundle branch block of the wide S type in addition   The P–R interval was also prolonged and P became bifid in Case 12 when seen in sinus rhythm two and five years later In Case 16, 2   1 A-V block was found only on one occasion

After the observations of Evans (1944) who found 2   1 block in 27 consecutive cases of auricular paroxysmal tachycardia, it is remarkable that among our 24 patients with repetitive auricular paroxysmal tachycardia only three had 2   1 A-V block   Admittedly the CR_1 chest lead was not applied, but in most of our records (e g , Fig 2A) it is obvious that it is a 1   1 and not a 2   1 rhythm   The slower auricular rate may be a partial explanation

(2) REPETITIVE AURICULAR FLUTTER

Repetitive flutter is very rare and few examples have been reported   Ritchie (1912) described one as intermittent auricular flutter, Semerau (1918) and Wolferth (1925) each reported two cases of intermittent impure flutter, and East and Bain (1936) one further case (Fig 135)   The physiological mechanism of impure flutter was explained by Lewis (1920) as a variation in the path, or in the speed, of the circus movement from cycle to cycle

Ordinary flutter in the repetitive form must be exceptional   We observed it in Case 8 with repetitive auricular paroxysmal tachycardia and 2   1 A-V block once, and then for a short time only

In our four cases of repetitive flutter the short paroxysms of 1–3 sec duration are always introduced by an auricular extrasystole, this is followed by more or less irregular auricular activity at a rate of 200–370 with a completely irregular ventricular activity of 120–200   In Case 28, in whom the paroxysms could be produced at will by swallowing (Fig 7), there is a waxing and waning of the auricular rate, the approximate distances of the auricular waves during an attack of 8 cycles being 34, 30, 12, 16, 18, 18, 28, 30, and 34 hundredths of a second, corresponding to an auricular rate 180–370   The paroxysms in Cases 26, 27, 28 are followed by a pause, but not in Case 25 (Fig 8)   Case 28 in other records on the same occasion had an almost regular auricular tachycardia (or flutter) with 2   1 block

In the only instance of repetitive auricular fibrillation (Fig 9) the paroxysm in lead II is introduced by an auricular extrasystole, followed by another which initiates auricular fibrillation   Lead I of the same record shows auricular fibrillation, lead III sinus rhythm with auricular extrasystoles   The history favoured the diagnosis of repetitive auricular fibrillation,
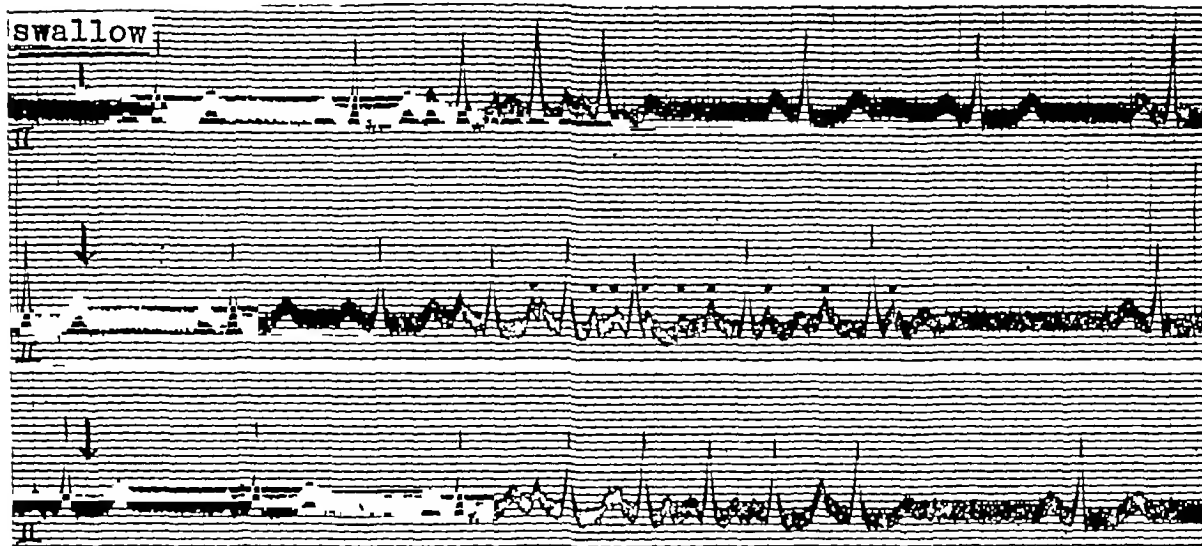
FIG 7 —Repetitive flutter, each paroxysm on swallowing   Case 28   Waxing and waning of auricular rate from 340 to 200 (dotted), ventricle irregular 200–100

FIG 8 —Repetitive flutter   Case 25   Auricular rate 380, slightly irregular, ventricular rate 160, irregular CR₁ chest lead   flutter waves

but the only record obtained of it is that here described   We have since seen another case of this kind with a similar electrocardiogram

(3) REPETITIVE NODAL PAROXYSMAL TACHYCARDIA

Though Case 1 was once seen in inferior nodal tachycardia, and isolated nodal extrasystoles occasionally appear in records of repetitive auricular paroxysmal tachycardia, repetitive nodal paroxysmal tachycardia itself is rare and only two examples were found

Case 30 shows regular nodal rhythm at a rate of 64, with occasional sinus beats while at rest   Sinus rhythm at rest was recorded only once during two years of observation Moderate effort produced nodal tachycardia at a rate of 130–140 with no visible P waves In Case 31 an inverted P follows R at a short distance, and gradual slowing occurs at the end of paroxysms (Fig 10)

FIG 9 —Repetitive auricular fibrillation   Case 29   Lead I   auricular fibril-
lation   Lead II   auricular extrasystole initiating period of fibrillation
Lead III   normal rhythm with auricular extrasystoles
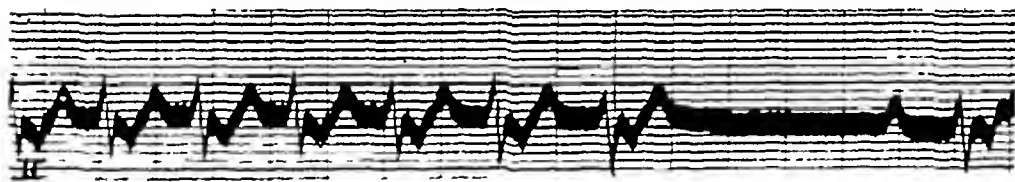
FIG 10 —Repetitive nodal paroxysmal tachycardia   Case 31   End and beginning of paroxysm
P–R interval, 0 24 sec after paroxysm

(4) REPETITIVE VENTRICULAR PAROXYSMAL TACHYCARDIA

Case 32 sometimes showed ventricular paroxysmal tachycardia with uniform ventricular complexes at an approximate rate of 200 and an auricular rate of 150 (Fig 11A), and sometimes multiform ventricular extrasystoles in groups separated from each other by one or two sinus beats (Fig 11B)   Case 33 had regular ventricular tachycardia at a rate of 120 when seen twice in 1943 and once in 1944   Under digitalis treatment sinus rhythm reappeared for a short time, a few days later, however, in spite of continued digitalis treatment, runs of ventricular extrasystoles were again found, and after one month these repeated runs were still present (Fig 12)   Extrasystoles of different origin can be seen in the records of Case 39, but runs of ventricular tachycardia are always produced by the same interpolated ventricular extrasystole and are not followed by a pause (Fig 13A and B)   Case 38 (Fig 14) with incessant bouts of irregular ventricular tachycardia at a maximum rate of 260, the highest in the series, was well and free from attacks when seen nine years later at the age of 69   The irregularity is even more obvious in Case 40 (Fig 15) where retrograde conduction is evident as it is in Case 33 (Fig 12) and Case 34   Except for Case 37, who died three years later, Case 40 is the only one with an enlarged heart and an abnormal cardiogram which here showed an inversion of T I of the sinus beat (Fig 15)   In all other records of this series the intervening sinus beats were normal and even during prolonged repetitive paroxysmal tachycardia the T of the sinus beats never seemed to change from upright to inverted   This is surprising in

A
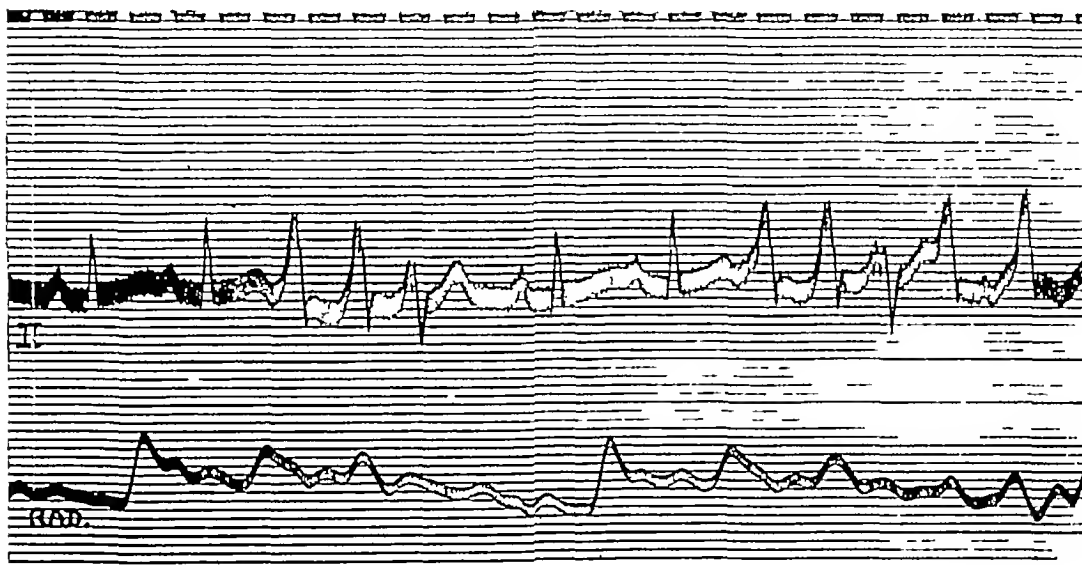
B

Fig 11 —Repetitive ventricular paroxysmal tachycardia (R V P T) Case 3 (A) Run of ventricular tachycardia, rate 240, almost regular, auricular rate 150 (B) Run of multiform ventricular extrasystoles at a similar rate, but irregular
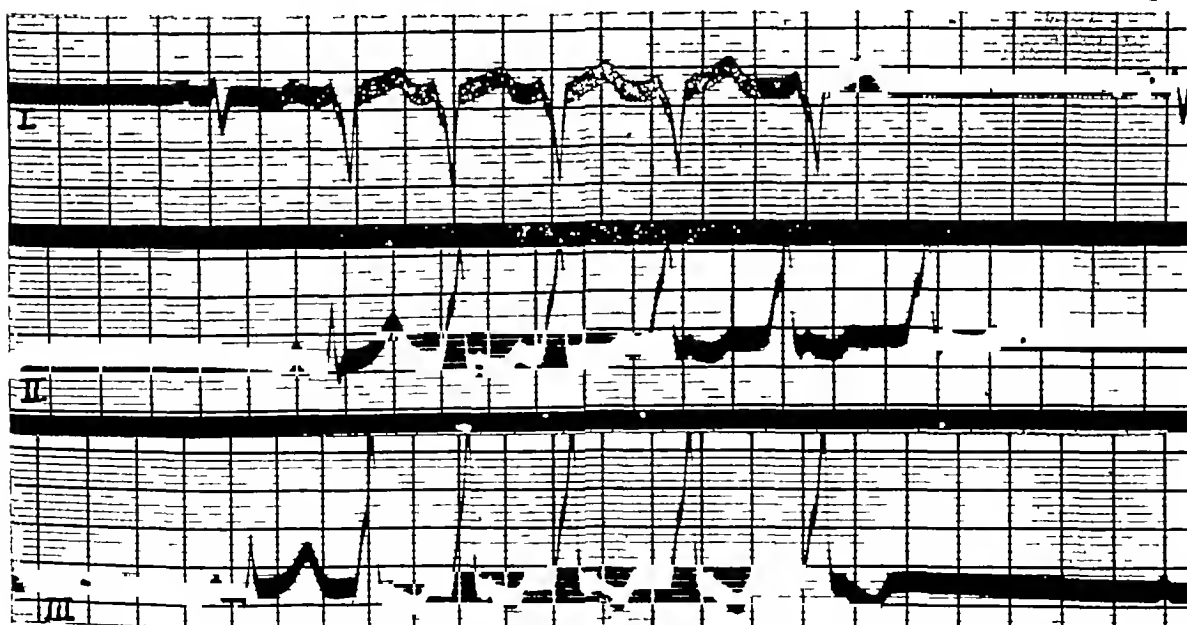
Fig 12 —R V P T Case 33 Gradual waning of ventricular rate from 140 to 110 Retrograde auricular conduction seen in leads II and III

view of the frequency with which T inversion during normal rhythm following prolonged paroxysmal tachycardia has been reported

THE NATURE OF THE CONDITION

Although the single beats of ordinary paroxysmal tachycardia closely resemble those of extrasystoles, the relation between the two is not as close as it may seem   Thus, extrasystoles are the most frequent of arrhythmias while paroxysmal tachycardia is uncommon   Further the majority of patients with ordinary paroxysmal tachycardia do not show extrasystoles in their normal rhythm   Campbell and Elliott (1939) found them in only 16 cases of their 42 cases with recorded paroxysms, and then they were often of a type different from the beats constituting the paroxysm   Isolated ventricular extrasystoles were found between attacks both of supraventricular and ventricular tachycardias

In repetitive paroxysmal tachycardia short spells of extrasystoles, varied in form and irregular in rhythm, often recur constituting tachycardiac runs   These, however, are not the only constituents in repetitive paroxysmal tachycardia, even more often there are typical short paroxysms of tachycardia with all the beats similar in form and exactly like ordinary paroxysmal tachycardia except in their brevity and constant recurrence   The rhythm is mostly regular, though during brief and low-rate paroxysms arrhythmia (? sinus) may be found (cf "nomotopic tachycardia," Maddox, 1937)   Many years after the repetitive paroxysmal tachycardia has ceased, frequent single extrasystoles are still often to be found As we see it, repetitive paroxysmal tachycardia provides a connecting link between extrasystoles and ordinary paroxysmal tachycardia, because it is composed both of runs and salvos of extrasystoles and of short ordinary paroxysms   Lewis (1909) expressed the same view about his relevant case of paroxysmal tachycardia already cited, and Katz (1946) illustrates the common genesis of extrasystoles and paroxysmal tachycardia in published records (Fig 385, 386, 391, 395, and 396)   Similar links can be established between auricular extrasystoles —e g , repetitive auricular tachycardia—and auricular flutter and fibrillation   In Case 20 short periods of flutter are mixed with the repetitive runs of auricular tachycardia, in Case 28 auricular paroxysmal tachycardia was recorded at a time when the patient exhibited repetitive impure flutter, and the reverse occurred in Case 8 with repetitive auricular tachycardia and 2 1 A-V block who once showed pure flutter   Case 14 with repetitive showers of multiple auricular extrasystoles was twice recorded in auricular fibrillation   Repetitive flutter was always introduced by an auricular extrasystole, and so was repetitive auricular fibrillation in our only case   Repetitive auricular tachycardia illustrates better than any other condition the interdependence of arrhythmias   The relationship between the single groups may at times be so close that electrocardiographic distinction may be impossible—as it often is between auricular paroxysmal tachycardia with 2 1 A-V block and flutter (Evans, 1944)

Ætiology   Repetitive paroxysmal tachycardia apparently is not due to inflammatory, degenerative, or toxic causes   Though two of our patients gave a history of rheumatic fever or chorea, none had rheumatic heart disease, and the infections preceding the arrhythmia in a few, e g , diphtheria in Case 31, glandular fever in Case 7, may have been incidental Only one of the nine with repetitive ventricular tachycardia had hypertensive heart disease, and none of them had angina pectoris in any form   Heavy smokers and drinkers were scarce in our series   An objection to organic heart disease as a cause is that the basic cardiogram between the paroxysms and after an interval of years, with two exceptions always remained normal   In three cases an abnormal thyroid may have been the source of this arrhythmia Case 32 was found to have a goitre with slight hyperthyroidism when seen five years after she had been under observation for repetitive ventricular paroxysmal tachycardia   Case 15, with the auricular form, had an enlarged thyroid   Case 14 had a slight thyroid enlargement and a fine tremor, and mild hyperthyroidism was diagnosed by us and the next year by another

observer who proposed a subtotal thyroidectomy which was refused   the next year paroxysmal fibrillation appeared in addition to repetitive paroxysmal auricular tachycardia as before

The relative rarity of paroxysmal tachycardia of any type, its occurrence in infancy, childhood, and early adult life, its occasional association with congenital heart disease (Case 8), in default of any other convincing cause at least permits us to suggest that it may be due to a congenital peculiarity in the conducting (specific) system of the heart   A recent case of congenital paroxysmal tachycardia diagnosed during fœtal life and confirmed after birth is described by Garvin and Kline (1947)   Congenital heart block is already fully accepted   The current opinion about the short P–R bundle branch block condition (the so-called W P W syndrome) is that it depends upon a congenital anomaly in the conducting system, and if so the high incidence of paroxysmal tachycardia in that syndrome points to a common congenital ætiology for both   That is also the view of Fine and Miller (1940)   Admittedly the disturbance may arise in the nervous control of the heart and possibly from a congenital anomaly there   The relation to emotion or exertion (Cases 19, 30), and in one particular instance to swallowing (Case 28) (Fig 7), intimates that the mechanism is at least under nervous control

Diagnosis   When first clinically examined a patient was often thought to have auricular fibrillation or flutter, though sometimes the unusual nature of the case was suspected from the pulse   In general the condition cannot be recognized clinically, and the diagnosis rests upon the cardiographic recording of constantly recurring short paroxysms of tachycardia separated from each other by single or several sinus beats, sometimes more   This paroxysmal state continues for weeks or months or even years   In a proportion including some of the ventricular variety, there are also numerous short runs or salvos of multiform extrasystoles, irregular in rhythm   Contrary to the opinion of Froment (1932) we think that the cardiogram of such cases (Fig 11B) in no way differs from that of " grave " or " terminal " ventricular tachycardias except that normal sinus beats are also in evidence   Sometimes short extrasystolic runs alone constitute the repetitive brief paroxysms

Certain allied conditions will be discussed shortly

(1) *Persistent paroxysmal tachycardia* (or ectopic auricular tachycardia) seems to be interminable and every record shows nothing but " paroxysmal tachycardia ' for months and years   Such has been described by Weiss and McGuire (1936)   Of this condition we have records of two cases, both children, one (P T) aged 2½, and the other (R W) aged 6 years In the first the   paroxysm ' seems to have persisted for almost three years at a regular rate of 170 and the cardiogram has always shown inverted P I, bifid P II, and diphasic P III   in the second with a similar observation period and rate there was always a diphasic P I with inverted P II and P III   Prolonged observation in hospital was possible in the second child,
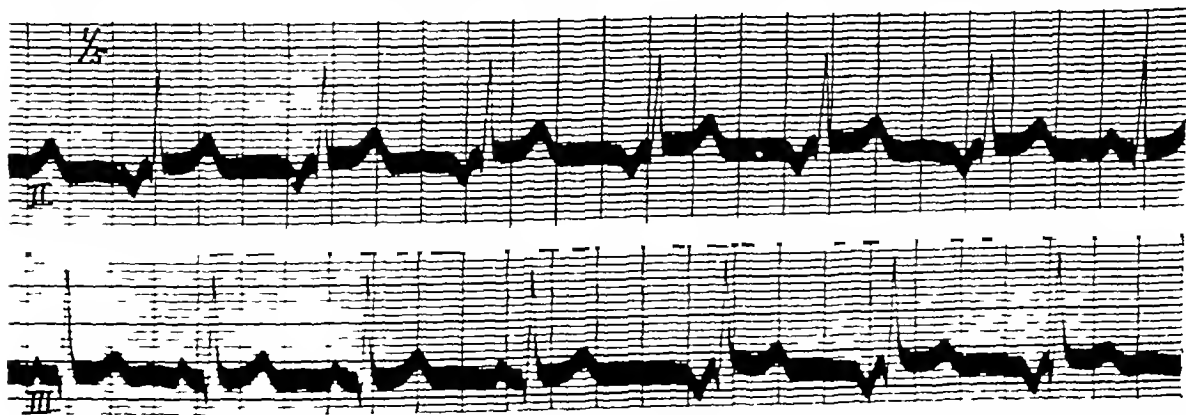
Fig 16   Auricular rhythm   Case G F   Change in rhythm   inversion of P and slight shortening of P–R interval—without change in rate

and under digitalis treatment sinus beats and transient sinus rhythm appeared, but the ectopic tachycardia recurred as soon as the effect of the drug wore off   Herson and Willington (1947) made a similar observation   In Cases 11, 15, and 33, digitalis broke up the apparently persistent paroxysms into repetitive paroxysmal runs which persisted after treatment was stopped   Thus the difference between persistent and repetitive paroxysmal tachycardia based on the frequent appearance of sinus beats in the latter, is not great because persistent paroxysmal tachycardia under hospital observation and digitalis. treatment can often be transformed, at least temporarily, into the repetitive variety

It is worthy of note that runs of irregular and multiform extrasystoles always seem to be short and do not in nature compose the long attacks that characterize ordinary paroxysmal tachycardia as distinct from repetitive paroxysmal tachycardia

(2) *Auricular rhythm without tachycardia*   The term auricular rhythm is here used in contrast with sinus rhythm, and it is comparable with nodal rhythm   It comprises instances in which the P of the sinus beat suddenly changes to an abnormal P without any increase in rate   This condition, described by Scherf and Harris (1946) as " coronary sinus rhythm, was observed in three cases, not included in our series for there was no tachycardia during the abnormal rhythm marked by the sudden inversion of P I and P II (Fig 16)   The close relationship of auricular rhythm to repetitive paroxysmal tachycardia is shown by our Case 12 (vide Fig 1 (C) in Barker *et al* 1943), and the one of Maddox (1937), in both of them an ectopic P identical with the one during paroxysms continued when the paroxysms were over and the rate was slow   Normal sinus rhythm was not seen

(3) *Sinus arrhythmia*   The short and low-rate irregular paroxysms of repetitive auricular paroxysmal tachycardia may be mistaken for sinus arrhythmia   Distinctive features are the ectopic P waves of all but the first complexes of the runs, and the pause that follows the runs (Fig 1)

Course, Treatment, and Prognosis

The case notes (see appendix) will illustrate the course of repetitive paroxysmal tachycardia Children often grow out of it at the time of adolescence   The state of paroxysms subsided in Cases 1 and 13 at the age of 14 and 15 years, and Case 11, observed in a state of paroxysms for three months when 11, was found in normal rhythm four years later   Case 5 forms an exception, observed for sinus tachycardia since the age of 11, he had repetitive auricular paroxysmal tachycardia when 15 and still had it when last seen at the age of 18   Among 14 adults who could be followed up, six (Cases 9, 14, 17, 18, 20, and 33) had repetitive paroxysmal tachycardia one, four, and five years after it was first detected, while eight had either a normal cardiogram when re-examined or had stated they were free from palpitation when questioned by letter   Among them were Cases 32, 35, 36, and 38 with repetitive ventricular tachycardia in whom the state of paroxysms was known to have lasted from $2\frac{1}{2}$ years (Case 32) to 4 months (Case 35)   The state of paroxysms in most patients did not cease abruptly, but the paroxysms gradually became less frequent, then occurred at long intervals, eventually perhaps disappearing altogether

The disability arising from repetitive paroxysmal tachycardia differs according to the patient, and the rate and duration of the paroxysms   Children tolerate almost continuous tachycardia at a rate of 160–180 surprisingly well, being generally symptomless, and so do adults if not subjected to excessive physical strain   Case 15 sustained successfully the operation of bilateral salpingo-oophorectomy complicated by postoperative bronchopneumonia, while in the paroxysmal state with a pulse rate of 120–160

The course and duration of repetitive paroxysmal tachycardia cannot be much modified by treatment, though the paroxysms disappeared in Case 6 after two months' quinidine   An almost continuous ventricular tachycardia in Case 33 and a continuous auricular tachycardia in Cases 11 and 15 were transformed into a repetitive one by digitalis   Unsuccessful attempts

with both digitalis and quinidine were far more numerous (Cases 1, 3, 4, 13, 7, and 12)   Nor had vagal compression and deep breathing any effect when tried during prolonged paroxysms

The prognosis in general is certainly better than one might at first suppose   Though therapeutic attempts usually fail there is good reason to expect that in time the state of recurrent tachycardia will pass   Meanwhile most patients are able to live an almost normal life provided they avoid great physical activity   Our series of prolonged observations includes only three cases where heart disease was already evident, of these, two were little affected but one of them (Case 37) was mortally aggravated by repetitive tachycardia—ventricular in this case

Summary

The name   repetitive ' is here applied to a special variety of paroxysmal tachycardia in which short paroxysms separated by sinus beats constantly recur over months or years

Forty new cases of repetitive paroxysmal tachycardia have been collected, nineteen of them with prolonged observation periods ranging from two months to eighteen years, and their clinical and electrocardiographic features were studied   Ages extended from 4 to 75 years, with two-thirds of the patients (including seven children) under 40   Males were affected twice as often as females

The usual symptom was palpitation, and four patients with the ventricular form had syncopal attacks in addition   With few exceptions the disability caused by the recurrent paroxysms was surprisingly slight   Fourteen patients—seven children and seven adults—had no symptoms, and all but one of these had repetitive auricular tachycardia

Of the forty cases only three had evidence of organic heart disease   One case with the ventricular form had hypertension and cardiac enlargement, another had cardiac enlargement of unknown origin, the other with the auricular form had congenital heart disease   Toxic goitre was found in two with the auricular form and in one with the ventricular form   Two gave a rheumatic history but had no rheumatic heart disease

An irregular pulse was the only clinical sign   The diagnosis was based on finding in a patient at numerous consecutive examinations a particular kind of electrocardiogram   This showed on almost every occasion, short paroxysms of tachycardia composed of several beats or more, and separated by normal sinus beats   The electrocardiogram in its rhythm was divided as follows

(a) Repetitive auricular paroxysmal tachycardia, 24 cases   In 16 there were short runs of the ordinary pattern, in 5 cases there were in addition salvos of multiform auricular extrasystoles which in 3 of these formed alone the brief irregular paroxysms   The rate was lower than in ordinary paroxysmal tachycardia, being on the average 150 in children and 130 in adults

(b) Repetitive auricular flutter, 5 cases   This differed from ordinary flutter in that the auricular rhythm was irregular (impure flutter)   One here included was probably fibrillation

(c) Repetitive nodal paroxysmal tachycardia, 2 cases

(d) Repetitive ventricular paroxysmal tachycardia, 9 cases, in brief, repeated paroxysms, identical with ordinary ventricular tachycardia (including the grave variety) in respect of the electrocardiogram, except that the sinus beats between paroxysms were physiological, giving no evidence of organic heart disease

Repetitive paroxysmal tachycardia provides a connecting link between extrasystole and paroxysmal tachycardia because it may be composed both of runs of extrasystoles and of short ordinary paroxysms   The extrasystolic type is irregular and the paroxysmal tachycardia type is more often irregular than is ordinary paroxysmal tachycardia   The ætiology of repetitive paroxysmal tachycardia is unknown though something can be said for the view that it arises from a congenital anomaly of the conducting system

The paroxysmal state is uncertain in its duration, but it often subsides   In children it

may last until adolescence, in adults it may last for years and then disappear as it did in 8 out of 14 cases long observed   The prognosis as regards disability and length of life is good both in the auricular and the ventricular form, naturally there are exceptions   Quinidine may be tried especially in the ventricular form, but the results are meagre, digitalis is also disappointing, neither is likely to terminate the state of paroxysms   Repetitive paroxysmal tachycardia may be regarded as a distinctive disorder of rhythm rather than a cardiac disease of consequence

ILLUSTRATIVE CASES

List of Abbreviations

A Ex   = auricular extrasystole(s)
A P T   = auricular paroxysmal tachycardia
B B Bl   = bundle branch block
B P   = blood pressure
EC   = electrocardiogram(s)
N R   = normal rhythm (sinus rhythm)
R A P T   = repetitive auricular paroxysmal tachycardia
R V P T   = repetitive ventricular paroxysmal tachycardia
V Ex   = ventricular extrasystole(s)
V T   = ventricular tachycardia

Case 1, aged 6

Repetitive tachycardia in a boy aged 6, almost continuously present for ten years without symptoms or signs other than a rapid irregular pulse   Electrocardiogram (EC) almost always showed runs of regular auricular tachycardia interspersed with sinus beats, also groups of multiform auricular extrasystoles Digitalis and quinidine unsuccessful   Normal school life, then gradual and spontaneous disappearance of the arrhythmia after the age of 16   Well and at work free from paroxysms at the age of 27 (21 years' observation)

History   He was a twin and weighed only 4½ lb at birth   He had always been fit until the last few weeks when his mother noticed that the heart was beating fast, and his father, a doctor, found the pulse to be uncountable   The child did not complain and had always been particularly active

Examination (1925)   Well-developed, of good colour, not distressed   No abnormal signs except for irregular tachycardia varying from 120–180   Heart sounds clear, no cardiac enlargement on radioscopy   EC (Fig 2)   short runs of A P T and multiple A Ex interspersed with occasional normal beats

Course   From 1925 till 1943 he was examined at frequent intervals, he was also under close observation during the first five years by his father, who for one year charted the pulse three times a day   The child had hardly a day without paroxysms or very frequent extrasystoles, so that it was uncommon to find the pulse completely regular, neither absolute rest in bed nor moderate exertion made any difference, and during sleep at times the pulse was found as irregular   Quinidine had no effect when given for two months, nor had digitalis when given for three weeks, both in moderate doses   Climatic change was without effect, for the pulse was as irregular in the Highlands as it was at the seaside   Intercurrent diseases left the paroxysms unaffected   in 1926 during a period of acidosis with renal glycosuria, pyrexia, and vomiting, the paroxysms were as before   From 1929 onwards he lived an almost normal life for a schoolboy of his age   He took part in light games, drill, and physical exercises, first at public school, later at the university, avoiding only hard games and competitive sports   In 1932, when 13, the paroxysms became less frequent, and when seen in 1933 there were no extrasystoles or paroxysms   He still had occasional palpitation, and in 1935 runs of paroxysmal tachycardia were again recorded   The EC was normal during the last two visits in 1939 and 1943 when he was working as a curate and only occasionally had rapid and irregular heart action   EC were recorded first at monthly, later at 3–6 monthly periods till 1932, once in 1933, twice in 1935, and again in 1939 and 1943   Outside the paroxysms they are remarkable for the constant pattern all

through the 18 years of recorded observation and except for Q III are normal   During the paroxysmal attacks either runs of multiform A Ex , mostly 3–5 in number, follow each other at irregular intervals at a rate of 160–180, or longer stretches of regular A P T composed of the same elements persist at a rate of 140–150   These two features can be found side by side on the same record (Fig 2)   Once a short paroxysm of nodal tachycardia was recorded   In January 1947 he was reported to be well and at work, and he had no recurrence of palpitation,   this was at the end of 21 years' observation

Case 2, aged 7

Arrhythmia found on routine examination in a boy of 7, constantly present till the age of 12   No complaints and no organic heart disease   EC almost always showed repetitive auricular paroxysmal tachycardia with 2   1 A-V block and an auricular rate of 300   After 5 years, spontaneous reappearance and persistence of sinus rhythm with P–R interval of 0 24 and right bundle branch block in the EC

History   Tonsils and adenoids removed 8 months ago   No complaints, energetic, not short of breath

Examination (October 1930)   Short systolic murmur at the apex   No cardiac enlargement Pulse completely irregular, at first regarded as extreme sinus arrhythmia   EC short and long runs of A P T interspersed with periods of normal rhythm   During A P T the ventricular complex is modified and resembles that of right bundle branch block,   closer inspection shows the deep S in lead II to be due to an inverted P and thus during paroxysm 2   1 A-V block persists with an auricular rate of approx 300 and a ventricular rate of 150

Course   Under observation (Dr Maurice Campbell) in Guy's Hospital in November and December 1930, because of otitis media   EC were always the same, a basic rate of 90–110 suddenly interrupted by a run of A P T at a ventricular rate of 140–170   Effort and deep breathing had no effect on the paroxysms   Seen at frequent intervals from 1930–5,   transient sinus rhythm was recorded only twice, the next record on the same day again showed A P T   In 1936 sinus rhythm seemed to be re-established at a rate of 75,   P–R of 0 22 sec and right bundle branch block (deep S type) persisted in the EC   He felt well and did not complain

Case 3, aged 22

Young woman complaining of attacks of faintness, actual faints, and palpitation for five years Normal heart except for irregular tachycardia   EC showed repetitive auricular paroxysmal tachycardia During five years of observation only twice was transient sinus rhythm recorded   All treatment failed

History   Five years ago " fainting " attacks rarely producing unconsciousness, in hospital for 3 weeks   For 3 years frequent recurrence of faint feelings accompanied by palpitation,   also slightly breathless on exertion

Examination (March 1931)   Varying, irregular pulse, 80–110   B P 125/70   Clear heart sounds, radioscopy normal   EC sudden runs of slightly irregular A P T at a rate of 130–140, preceded by a normal beat and followed by a pause   P II and P III inverted

Course   Heart Hospital in-patient from March till July 1931   During this period the pulse was hardly ever found to be regular, though the rate occasionally dropped to 70   Usual rate at rest 120–140   Quinidine, quinine, digitalis, and atropine had no effect on the rhythm   EC were almost always of R A P T , when the paroxysms were short the rate was irregular because of slowing towards the end, when they were long it was regular, 130   Normal rhythm was recorded only three times, at a rate of 80–100   Seen again in February 1932 because of fainting in the street while having palpitation, EC was found unchanged except for a prolongation of the P–R interval to 0 22 sec towards the end of the paroxysms   Under observation as out-patient from April 1935 till January 1936 still complaining of giddiness and faintings,   heart and B P were again found normal, and EC showed R A P T on every occasion

Case 4, aged 20

Man, aged 20, discharged from the Army for D A H   complaining of palpitation for many years Normal heart except for arrhythmia, rate 120   EC showed repetitive runs of auricular paroxysmal tachycardia   During 5 years of observation not once seen in sinus rhythm   Quinidine ineffective

History   Discharged from the Army in 1918 because of disordered action of the heart   Complains of continuous palpitation, breathlessness, and slight cough, but at work

Examination (April 1920)   Pulse 130, regular   Heart sounds normal   No cardiac enlargement   EC , A P T , 132, regular, P II and P III inverted

Course   Observed as an out-patient till February 1925   EC taken first at monthly then at three-monthly intervals always showed either continuous, regular A P T at a rate of 120–130, or short runs of the same pattern preceded by a normal beat and followed by a pause of 1 2 to 1 4 sec   Occasional normal beats were followed by a blocked A Ex , at one time single V Ex were seen   Quinidine was ineffective

Case 6, aged 30

Woman, aged 30, complaining of palpitation   No heart disease   EC during 9 months' observation always showed repetitive runs of auricular paroxysmal tachycardia and groups of multiform auricular extrasystoles   Disappearance of paroxysms under quinidine

History   Frequent attacks of sudden palpitation

Examination (December 1938)   No heart disease   Radioscopy normal   EC runs of nodal and auricular Ex , some with aberrant ventricular complex, at times periods of irregular ventricular activity at a rate of 170 with no visible P waves (? fibrillation)   Paroxysm often begins with a nodal beat and is always followed by a pause (Fig 4)

Course   Observed as an out-patient till August 1939 at monthly intervals, from then till June 1942 at six-monthly intervals   EC always similar, with shorter or longer runs of Ex and A P T till May 1939   Quinidine was tried and when seen in July she had only single A Ex , quinidine 3 grains t.d s continued for three months, from August 1939 onwards she was only seen in sinus rhythm, though still having occasional palpitation

Case 8, aged 11

Boy of 11 with congenital heart disease, probably atrial septal defect, and a rapid irregular pulse EC repetitive auricular paroxysmal tachycardia with 2   1 A-V block, auricular rate 200   Persistence during 2½ years of observation, once in flutter, never in sinus rhythm   Quinidine reduced auricular rate, otherwise ineffective

History   Delicate from birth, as a baby had blue lips, and as a child was unable to play games because of shortness of breath   When aged 5, school doctor sent him to special school because of heart disease

Examination (February 1924)   High colour and slight cyanosis of lips, no dyspnœa   Pulse 100, very irregular, with frequent long pauses   Soft systolic murmur loudest at the pulmonary area and over 3rd and 4th left spaces, no thrill   Pulmonary second sound heard   Radioscopy prominence and increased pulsation of pulmonary artery with large hilar branches, right ventricle enlarged   EC runs of A P T with P II and P III inversion, 2   1 A-V block   Auricular rate 180–220 irregular ventricular rate half   Very occasional aberrant beats

Diagnosis   Congenital heart disease, probably atrial septal defect

Course   Out-patient (National Heart Hospital) from February till December 1924, seen at frequent intervals, EC always the same   In-patient from January 31st till March 14th, 1925   During this period of close observation not once was sinus rhythm recorded and the paroxysmal state persisted all the time   The auricular rate was usually 190 with 2   1 block, only occasionally were higher grades of block recorded   The short paroxysms usually ended with a pause of 1 2 sec or less, succeeded by a sinus beat and then a new run   The P–R interval of the sinus and paroxysmal beats was identical and slightly prolonged to 0 22 sec   Once a paroxysm of flutter was recorded, the auricular rate being 308, the ventricular half this and quite regular

Vagal pressure had no effect on the EC   *Exercise*, paroxysms became shorter, otherwise no effect Atropine, 1/100 of a grain subcutaneously, increased average auricular rate from 190 to 220   Quinidine reduced the auricular rate of 105 and abolished 2   1 block, but only temporarily

From January till October 1926 seen frequently as an out-patient, the same abnormal rhythm was recorded on every occasion

Case 14, aged 59

Man, aged 59 complaining of irregular heart beating   Pulse irregular, thyroid enlarged with mild toxic signs, no cardiac enlargement   During 3½ years of observation EC almost constantly showed runs

of multiform auricular extrasystoles at a rate of 140–160 *and irregular   Sinus rhythm was exceptional, transient auricular fibrillation twice recorded   Digitalis ineffective*

History   B P found raised 10 years ago when for the first time felt ' fluttering and quivering " in the chest at night   For three months missed beats, coupling, or else a completely irregular heart Feels fit and walks any distance

Examination (October 1942)   Pulse irregular, 70–80   B P 160/95   Normal heart sounds, no cardiac enlargement   Isthmus of thyroid gland easily seen, fine tremor of hands, toxic goitre suspected   EC (Fig 3) runs of A Ex (8–10) of different origin at an irregular rate 140–160, followed by pause   Basic rate, 66 regular

Course   June 1942 observed at Liverpool Royal Infirmary (Dr Wallace-Jones)   EC invariably the same   B M R +27 per cent   Iodine treatment begun, reported August 1943, less palpitation under iodine, but EC unchanged   Subtotal thyroidectomy considered but not performed   From May 5th till June 9th, 1944, in Manchester Royal Infirmary (Prof Crighton Bramwell), diagnosis of toxic goitre doubted   B M R +5 per cent   Among 28 EC there recorded, 23 show runs of multiform A Ex sometimes interspersed with sinus beats, 3 sinus rhythm, and 2 auricular fibrillation This last appeared under digitalis which was ineffective in reducing the paroxysms but increased the number of blocked A Ex

Seen again in July 1944, February and September 1945, and March 1946, paroxysms recorded on each occasion

Case 18, aged 18

Healthy and active man of 18, no complaints   Referred by Medical Board because of irregular pulse This found at the age of 14 on routine examination   EC then as now, showed repetitive auricular paroxysmal tachycardia with Wenckebach periods

History   Played games at school   On admission as naval cadet, aged 14, doctor noticed irregular pulse   EC (inspected) then showed short runs of A P T similar to the one described below   Completed full physical training of cadet, and never complained of palpitation   Referred by Medical Board because of irregular pulse

Examination (February 1947)   Pulse very irregular with series of rapid beats then pause, persistent, no change on exertion   B P 130/80   Normal heart sounds   X-rays, no enlargement EC continuous short runs (3–7 beats) of A P T at a slightly irregular rate of 120–130 with gradual increase of P–R interval from 0 18 to 0 24 (Fig 5A)   The first two P waves of the paroxysms appear normal, and are small and upright, then P changes, often gradually, to flat-diphasic (lead II)   The paroxysm sometimes ended with a blocked P wave, always followed by a pause of varied length

Case 25, aged 34

Woman, aged 34, complaining of palpitation   Irregular pulse found with short paroxysms of tachycardia, otherwise normal heart   Three years later EC showed repetitive flutter

History   Sudden attacks of rapid heart-beating for a few seconds, minutes, or hours   More frequent when lying, occasionally a dozen a day   Referred by a doctor because of extrasystoles

Examination (October 1941)   Pulse 120 with occasional irregularities   At times 5–6 beats in paroxysms at a rate of 160–180   Otherwise no cardiac abnormality   No EC then recorded

In December 1944 she had the same complaints   EC basic rate 90–100, regular, with tall P II Sudden bursts of slightly irregular, apparently independent ventricular activity of 200, lasting for 7–12 auricular cycles, after which the normal rhythm resumes without intervening pause   CR₁ typical flutter waves (Fig 8)

Case 30, aged 22

Woman of 22 had irregular heart when aged 6, normal adolescence   Palpitation on effort   EC during two years of observation always showed nodal tachycardia on exertion, nodal rhythm or sinus rhythm at rest   No other signs of heart disease   Spontaneous improvement with little acceleration on exertion, but persistence of abnormal rhythm

History   When aged 6, heart was found irregular   she was allowed to play games only after the age of 13   For 2–3 months, palpitation and increasing dyspnœa on exertion

Examination (July 1944)   On standing, pulse 120, regular, after ½–1 minutes irregular, then 76, regular   Exercise increases rate to 130, persisting for several minutes   No other abnormal signs   radioscopy normal   EC nodal tachycardia

Course   EC were recorded first at fortnightly, then at monthly, later at three-monthly intervals from July 1944 till June 1946   At rest   nodal rhythm, no P waves visible, rate 60–70, regular   Sinus rhythm found only once   On exertion   nodal tachycardia, 130–140, regular, when rate drops few sinus beats appear   At the last examination there was sinus rhythm in lead I, nodal rhythm in leads II and III while at rest, nodal rhythm at a rate of 96 on exertion   She was then better and able to exert herself without much palpitation or dyspnœa

Case 32, aged 35

Woman, aged 35, complaining of sudden faintness and palpitation   Pulse rapid, irregular, otherwise normal heart   EC during 2½ years of observation constantly showed repetitive ventricular tachycardia and multiform extrasystoles   Quinidine ineffective   Ten years later mild toxic goitre, yet no recurrence of paroxysms

History   Well until one year ago when she collapsed in the street with sudden palpitation, weakness, and dizziness, many similar attacks since

Examination (April 1921)   Except for irregular pulse nothing abnormal   No cardiac enlargement on radioscopy   EC, R V P T, rate 220 reg, aur rate 150, reg   Shorter runs of 2–3 V Ex   Intervening sinus beats at a rate of 110 (Fig 11A and B)

Course   EC recorded twice in February 1922, June 1922, October 1923, always showed R V P T at a rate of 200–250   Quinidine at first reduced the number of attacks, but was later ineffective   Seen again January 1931, still complained of palpitation   Examination then showed small toxic goitre, with a pulse rate of 96   B P 160/90, slight tremor, normal heart on physical and radiological examination   EC showed N R except for single ventricular extrasystoles   She improved with rest and sedatives and the signs of toxic goitre subsided   When last seen in 1934, she felt well, single V Ex were still present in the EC

Case 33, aged 20

Man of 20, served as air pilot during the war, discharged from R A F because of heart disease   Complains of palpitations and fainting attacks   Normal heart except for tachycardia   Three EC during 10 months of observation as an out-patient showed regular ventricular tachycardia, rate 120   While in hospital and on digitalis, transient sinus rhythm appeared, followed by repetitive ventricular tachycardia, always present during the remaining 14 months of observation

History   Two years ago when volunteering for the R A F pulse was found " queer "   Examined several times before being accepted Grade 1   Trained as a pilot, apt for his duties, flying at times at 20,000 feet without oxygen   Tonsillitis 6 months ago, kept for 3 months in hospital where X-rays and EC were taken   Discharged from R A F because of " congenital heart disease "   Complains of frequent palpitation and dizziness   Fainted four times during the year while on parade

Examination (November 1943)   Pulse 110, reg   B P 105/80   Heart sounds normal   Radioscopy   full-sized heart within normal limits   EC, V T (Right B B Bl), 125 reg, no P waves seen   Five days later, EC similar

Course   Seen again September 1944, having frequent palpitation even at night, usually short attacks 1–2 min duration   EC, V T as before   Under observation at the London Hospital 9th October till 11th November 1944   V T persisted while at rest, rate 110–130   Under digitalis leaf 1½ grains t i d pulse became irregular and the rate decreased occasionally to 50 when the pulse became regular and the EC normal   Digitalis, 1 grain bis die, later t i d, successive EC always showed V.Ex singly or in short runs (3–5), at a rate of 120–130, preceded by a sinus beat and followed by pause with a basic rate of 90–96 (Fig 12)   One month later the EC was the same   In 1946 it was heard by chance that he had committed suicide

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A CASE OF PERFORATED DUODENAL ULCER AND CARDIAC INFARCTION

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The following case was thought to be of sufficient interest to be worth reporting because cardiac infarction seemed to follow within an hour of a perforated duodenal ulcer

A musician, aged 58 years, was admitted to Edinburgh Royal Infirmary, on 21/1/47   For six months he had experienced attacks of pain over the upper part of the sternum, crushing in character, and radiating to the shoulder and arm as far as the elbow on the left side   The pain was brought on by exertion, over-eating, excitement, and cold, and was relieved by rest, leaving the præcordium and the left arm numb   The attacks became progressively more severe, more frequent and more easily provoked by exertion

Three months from the onset he experienced a violent attack of sternal pain while at rest in bed, the pain was very severe, crushing in character, and radiated down the left arm to the fingers   It persisted all night but eased next day   He was not confined to bed at this time but remained in the house resting   During the following months he had several further attacks of pain, usually brought on by very slight exertion, such as washing or dressing   Electrocardiograms in November 1946, showed little abnormality in the resting records apart from left axis deviation, but conspicuous S–T distortion after exercise

The patient had suffered periodically from indigestion for 20 years   The attacks were characterized by pain and distension in the epigastrium, relieved by food and alkalis   A barium meal examination three years before had shown no abnormality

The family and social history was irrelevant

On examination he was of average height and build, anxious and worried, but without cyanosis or œdema   Clinical examination showed slight cardiac enlargement, a blood pressure of 180/110, faint heart sounds with gallop rhythm and a soft localized apical systolic murmur   Radiologically there was slight enlargement of the left ventricle

Abdominal examination showed no restriction of movement and no palpable mass or tenderness, but revealed guarding of the upper right rectus muscle   No other abnormalities were discovered on physical examination   The blood count was normal, the Wassermann reaction and urine examination negative   An electrocardiogram taken on 22/1/47 showed no gross abnormality

The clinical diagnosis was angina pectoris with severe coronary arterial disease   The patient was treated with complete rest in bed, a low residue diet, and half a grain of phenobarbitone morning and night, and glyceryl trinitrate tablets, 1/100 of a grain, taken when required

Progress   One week after admission his condition showed little change   even turning in bed brought on an attack of angina pectoris

At 12 noon on 29/1/47 he suddenly cried out with pain and lay completely motionless with flexed knees   His pulse was 90 a minute, the temperature 96° F , the respiration rate 28 a minute, and the blood pressure 90/50   Examination revealed entire absence of abdominal

movement on respiration and marked muscular guarding of the upper abdomen with extreme tenderness on palpation in the epigastrium   There was slight diminution of the liver dullness   The heart sounds were faint

The provisional diagnosis of perforated peptic ulcer was confirmed by a surgeon, but in view of the patient's poor general condition it was decided to adopt conservative rather than operative treatment

One hour later the patient stated that the pain had spread over the left side of the chest and down the left arm to his fingers   Previously immobile, he was now extremely restless and was bathed in a cold sweat   His pulse had risen to 100 a minute but respiration was unchanged in type and rate   The findings on abdominal examination were similar to those an hour before   Electrocardiograms at 1 20 p m and 4 20 p m showed changes indicative of recent cardiac infarction (Fig 1, B and C)

In view of the cardiographic evidence and the history of coronary disease, the provisional diagnosis of perforation was revised   It was assumed the patient had another cardiac infarction   He was treated with large doses of morphia and absolute rest

During the following six days the patient felt more comfortable, and had little discomfort after the first 48 hours   His pulse, however, continued fast (115–120), his gallop rhythm persisted, and basal crepitations were heard   There was now fever (101° F) with slight leucocytosis (10,800–11,400) and a fast B S R (24–30 mm Westergren)   Abdominal guarding and epigastric tenderness persisted   The cardiographic changes are discussed later and in more detail in the legend to Fig 1

On 6/2/47 the patient began to suffer from cardiac asthma   His pulse rate rose to 130 a minute and he developed coupled beats   The respiratory rate was 36 a minute   The apex beat was 3 cm outside the mid-clavicular line in the sixth left interspace   The heart sounds were feeble, there were many extrasystoles, and the apical systolic murmur persisted   Dullness on percussion and coarse crepitations were elicited on examination of the bases of the lungs   The patient was treated with continuous oxygen, aminophyllin, and morphia, but death occurred 10/2/47 from left ventricular failure

Electrocardiographic changes   The routine curve taken at 11 40 a m on 29/1/47 is of a type common in cases of myocardial disease of coronary origin, the conspicuous abnormalities being the T inversions in leads I and IVF   it was the same as earlier records

The record taken at 1 20 p m shows marked S–T shifts in chest leads indicative of " injury currents ", the nature of the changes with the history of pain rendered an ischæmic lesion likely   In the record three hours later QRS changes in limbs and chest leads, though slight, are apparent and were read as confirming infarction   The appearance of a small Q in the apical lead, together with the grossly aberrant QRS in leads C_2F suggested an early anterior infarction

The subsequent records are consistent with a developing infarct and the deep Q in the apical lead is characteristic of such a lesion underlying that electrode   The cardiographic diagnosis was a large coronary infarction involving *inter alia* the apical region

Necropsy   This was performed on 11/2/47

The pericardial sac contained 150 ml of blood-stained serous fluid   The visceral pericardium showed a loss of lustre over the anterior, postero-inferior, and apical regions of the heart   A fibrinous exudate and areas of fibrous thickening were present in the posterior part of the pericardial sac   The heart weighed 400 g , it was enlarged and showed generalized bulging of the apex and lateral aspect of the left ventricle   The anterior surface, apex, and lower part of the postero-inferior aspect of the heart were the seat of infarction, and internally this extended to the left ventricular wall and the interventricular septum   The myocardium was necrotic, thin, and covered with ante-mortem thrombus   The chambers and auriculoventricular orifices were dilated   The valves were healthy   The coronary arteries were
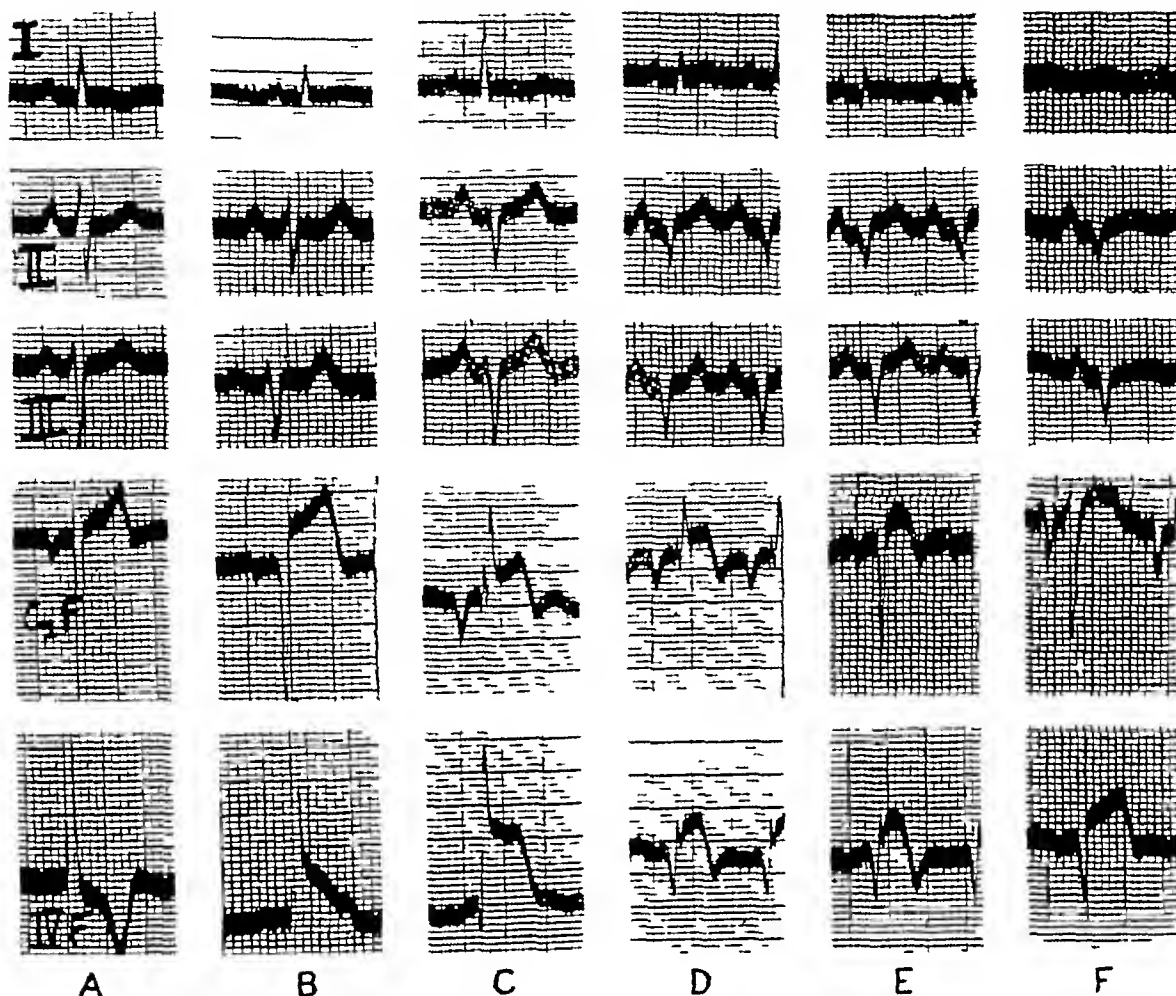
Fig 1

(A) 29/1/47, 11 40 a m   Sinus rhythm, rate 98 a minute   P–R interval 0 18 sec   left axis deviation   shallow inversion of T in lead I, upright T waves in leads II and III   The sternal chest lead (C₂F), shows a deep Q, and trace of S–T elevation and upright T waves   the T waves in lead IVF are deeply and sharply inverted

(B) 29/1/47, 1 20 p m   Sinus rhythm persists with P–R of 0 16 sec , and left axis deviation   The T waves in lead I are now low upright   In lead C₂F S–T elevation exceeding 5 mm in height has developed without changes in QRS or T   In the apical lead a tiny initial Q precedes the tall R, marked S–T elevation is present, and the inverted T waves have disappeared

(C) 29/1/47, 4 20 p m   In this record further changes are apparent, viz   disappearance of R in lead II increase in amplitude of R in lead I   diphasic T waves in lead I   gross changes in form of QRS in lead C₂F, with increase in size of vestigial Q in lead IVF   conspicuous "coronary" S–T–T segments in both chest leads

(D) 30/1/47   Sinus tachycardia rate approx   120 a minute   marked decrease in voltage of QRS an all limb leads   persistence of splintered upright QRS in lead C₂F   development of deep Q as main deflection in lead IVF   beginning inversion of terminal position of T in both chest leads

(E) 31/1/47   The principal changes from the last record are increased slurring of QRS in limb leads   shallow inversion of T in lead I   steep downward initial deflection in lead C₂F   and increase in depth of T inversion in both chest leads

(F) 10/2/47   This record shows further reduction in voltage in limb leads, involving QRS and T waves   return of initial deflections in lead C₂F to an rS pattern, and conspicuous if in the apical lead, with S–T elevation and upright T waves in both chest leads

atherosclerotic with greatly narrowed lumina   Recent ante-mortem thrombus was present in the descending branch of the left coronary artery   The aorta showed minimal atherosclerosis in its descending portion only

An abscess was present in the peritoneal sac, localized in the space between the hepatic

flexure, liver, and duodenum, walled off from the peritoneal cavity by dense fibrous adhesions and containing 200 ml of thick, foul smelling, greenish yellow pus   There was no generalized infection of the peritoneum   The abscess had originated from the perforation of a chronic peptic ulcer situated in the duodenum   The duodenum presented a peptic ulcer at the antero-inferior aspect of the first part immediately beyond the pylorus   The crater, measuring 12 mm × 5 mm had a hard sclerotic base and firm edges   A small perforation had occurred at the upper end, the lower extremity had eroded into the head of the pancreas

The appearance of the myocardial infarct and the localized peritonitis indicated they were both of about 14 days' duration

There were no other relevant findings apart from bilateral hydrothorax and congested and oedematous lungs

DISCUSSION

When the case is reviewed in the light of the post-mortem findings a number of interesting points arise

The Duodenal Ulcer   Despite the complaint of intermittent indigestion for 20 years, the symptoms were mild, and hardly suggestive of duodenal ulcer, still less of an ulcer eroding into the head of the pancreas, the constant dull boring pain characteristic of this complication of peptic ulcer was absent   X-ray examination three years ago had been negative   the ulcer may have developed since then, though its size and character suggested that it was of long standing

The Diagnosis and Sequence of Events   The sudden onset of epigastric pain without radiation to the arm, as had occurred on each previous attack of angina, the rigidity and tenderness in the upper abdomen, the diminution of liver dullness, the thoracic type of respiration with grunting expiration, the severe shock, the attitude and immobility of the patient, the relatively slow pulse and the furred tongue, all supported a diagnosis of perforated peptic ulcer, especially with a history of indigestion   The occurrence an hour later of pain in the chest with radiation to the left arm, intense restlessness, rapid pulse, enlargement of the heart, and characteristic changes in the electrocardiogram, all indicated the occurrence of a myocardial infarct

It is suggested that the perforation occurred at the time the patient suddenly cried out, and, due to the shock, low blood pressure, and poor flow blood, thrombosis occurred in the descending branch of the left coronary artery, that was already the seat of gross atherosclerosis   This was the cause of the extensive myocardial infarction, later causing left ventricular failure and leading to death

The Perforated Duodenal Ulcer   Post-mortem, the abscess was well localized between liver, hepatic flexure, and duodenum, and was completely walled off from the peritoneal cavity   If the patient had not died from coronary thrombosis the perforated ulcer would presumably have healed by conservative treatment, thus supporting the views of *Turner*, Taylor, and Visick, all of whom have advocated a conservative regime for these cases

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PAROXYSMAL HEART BLOCK IN BUNDLE BRANCH BLOCK

BY

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When a patient is suspected of having Stokes-Adams disease the electrocardiogram is of critical importance, particularly in respect of the auriculo-ventricular (A-V) conduction time Should this not be prolonged, the possibility of paroxysmal heart block remains, although the diagnosis of Stokes-Adams disease is uncertain without some degree of heart block recorded graphically It is not known how far major impairment of intraventricular conduction (bundle branch block) with a normal P–R interval predisposes to A-V dissociation, and, therefore, to Stokes-Adams attacks This matter is here considered

THE INVESTIGATION

In the records of the Cardiac Department of the London Hospital covering the last fifteen years were found 112 patients over the age of 40 years with heart block of a degree exceeding

TABLE I

CASES WITHOUT BUNDLE BRANCH BLOCK

P–R intervals tabulated with the time relation of electrocardiograms in normal rhythm and in A-V block

Case No	Age	Electrocardiograms (EC)		Degree of A-V block	Clinical comment
		Normal Rhythm P–R (sec)	Time in relation of EC in N R to EC in A-V block		
1	57	0 20	29 months before	C H B	" Giddy attacks " before the first EC later Stokes-Adams attacks For this analysis 0 26 sec is taken as the P–R interval
		0 26	9 weeks after		
		0 24	1 year after		
		0 22	4 years after		
2	63	0 32	Same day	C H B	Stokes-Adams attacks
3	61	0 17	9 months before	C H B	Epileptiform attacks for 8/12 before EC with normal rhythm
4	63	0 27	Same EC	2 1 H B	Referred from Neurological Dept Stokes-Adams attacks
5	62	0 28	Same EC	2 1 H B	Referred from Neurological Dept Syncope
6	49	0 30	15 months before	C H B	Stokes-Adams attacks
7	60	0 24	7 years before	C H B	Stokes-Adams attacks
8	43	0 19	Same day	C H B	Epileptiform attacks, referred from neurologist Five years later L B B Bl , C H B
9	41	0 22 QRS normal	6 weeks after	C H B R B B Bl	Stokes-Adams attacks continued when 3 years later EC showed normal QRS and P–R varying from 0 2 to 0 24
10	55	0 30	Same day	C H B	Stokes-Adams attacks
		0 40	10 days before		
11	52	0 30	13 days before	2 1 H B	Stokes-Adams attacks
12	46	0 29	1 month before	2 1 H B	Myotonia atrophica No syncopal symptoms

a prolonged P–R interval alone   Among these were 81 (62 with complete and 19 with partial heart block) from whom a cardiogram in normal sinus rhythm was never obtained and who were, on this account, discarded from the series   Thirty-one cases had cardiograms showing normal sinus rhythm as well as A-V block (partial or complete) at one time or another   Their ages ranged from 41 to 82 years   Those below 40 have been excluded because, in them, transient heart block may result from an acute infection such as rheumatic fever, whereas the condition now considered arises from ischæmic changes which are, in the main, progressive For purposes of analysis the 31 cases were separated into three groups

(1) A-V Block without Bundle Branch Block

In this category there were 12 cases   Their cardiograms in normal rhythm contained normal QRS complexes, although in the phase of A-V block one man (Case 9) showed right bundle branch block (*R B B Bl*)   Complete heart block (*C H B*) was demonstrated at least once in 8 of this group, and in the remaining 4 there was 2 1 heart block   Heart failure or cardiac infarction, either of which might impede conduction, was absent in all of them   In every case, except one with myotonia atrophica (Case 12), Stokes-Adams attacks preceded the cardiographic investigation   Details of this group are given in Table I

TABLE II

CASES WITH BUNDLE BRANCH BLOCK UNCOMPLICATED BY CARDIAC INFARCTION OR HEART FAILURE

Case No	Age	EC in Normal Rhythm		Time relation of EC in N.R., to EC in A-V block	EC showing A-V block	Clinical comment
		P–R (sec.)	Other features			
13	57	0 2	L B B Bl	Same EC	2 1 H B L B B Bl	Attacks of unconsciousness for 3 months before these EC
				17 days after and twice previously	C H B L B B Bl	
14	49	0 2	R B B Bl	8 months before	C H B, L B B Bl	3½ years' giddiness and faintness 22 months falling unconscious
15	63	0 18	R B B Bl (newer type)	6 days after	2 1 H B R B B Bl	First Stokes-Adams attack 15 months before these EC many observed in hospital
16	55	0 4	R B B Bl (newer type)	9 weeks before	2 1 H B R B B Bl	Stokes-Adams attacks
17	72	0 18	R B B Bl (newer type)	8 days after	C H B R B B Bl	Stokes-Adams attacks for 2 years before these EC
18	60	0 25	L B B Bl	8 months after	C H B L B B Bl	C H B, with Stokes-Adams attacks for 4 years after and symptoms 6 years prior to first EC
19	51	0 19	L B B Bl	Same day	2 1 H B L B B Bl	Stokes-Adams attacks for 3 weeks before the first EC
				8 months before	C H B R B B Bl	
20	55	0 2	L B B Bl	3 months after	C H B, L B B Bl	Several Stokes-Adams attacks in hospital Still alive 3 years later in C H B L B B Bl
21	54	0 18	L B B Bl	2 years before	2 1 H.B L B B Bl	Occasional Stokes-Adams attacks over a period of 5 years, P–R still less than 0 2 sec after last attack
22	46	0 2	L B B Bl	4 months before	2 1 H B L B B Bl	" Faints " for 3½ years before EC obtained to prove Stokes-Adams disease
23	51	0 18	L B B Bl	31 months before	C H B, R B B Bl (newer type)	C H B with Stokes-Adams attacks for 4 years, which include this interval of 31 months
24	60	0 22	L B B Bl	Same EC	3 2 H B L B B Bl	B P, 210/130 " Dizzy spells " No pain or failure

(2) *A-V Block with Bundle Branch Block*

This group also comprised 12 cases and they showed the cardiogram of bundle branch block   In sinus rhythm 8 had left bundle branch block (*L B B Bl*) and 4 *R B B Bl* of the type more recently recognized (Wilson *et al*, 1934, Evans, 1937)   A change of bundle branch pattern from left to right was seen in 2 cases (Cases 19 and 23) and in one (Case 14) from right to left with the record of A-V block   Particulars of this group are given in Table II

(3) *With Cardiac Infarction or Heart Failure*

This group contains 7 cases that were separated for two reasons

Cardiac infarction could not be excluded in 4 (Cases 25, 28, 29, and 30)   Such an accident, rapidly causing heart block, could happen regardless of the previous state of the genetic system   In this exclusion particular attention was paid to the history of pain because bundle branch block may mask the electrocardiographic signs of cardiac infarction (Wood, Jeffers, and Wolferth, 1935, Wilson, 1936 and 1945)   One of these patients with coronary pain (Case 30) was the only case of this group without bundle branch block

Heart failure was present in 4 patients (Cases 25, 26, 27, and 31)   There is evidence that this factor may precipitate heart block (Willius and Anderson, 1934), and accordingly these cases were separated from the first two groups, which, as will be seen, makes no material difference to the conclusions when the inclusive figures are compared

Before proceeding to the analysis of electrocardiograms it is necessary to consider the normal P–R interval   According to the Criteria Committee of the New York Heart Association (1943) the upper limit of the normal P–R interval in adults with normal heart rates is 0 2 sec   This arbitrary measurement is adopted for the present analysis   One other point

TABLE III

CASES COMPLICATED BY HEART FAILURE OR POSSIBLE CARDIAC INFARCTION

Case No	Age	EC in Normal Rhythm		Time relation of EC in N R to EC in A-V block	EC showing A-V block	Clinical comment
		P–R (sec)	Other features			
25	62	0 21	R B B Bl (newer type)	3 weeks after	3 1 H B R B B Bl	First Stokes-Adams attack 6 weeks before pain in chest after syncope on day of admission Several Stokes-Adams attacks observed in hospital ? Cardiac infarction Heart failure Died 1 yr later in C H B
26	59	0 23	L B B Bl	6 weeks before	C H B L B B Bl	Heart failure from mitral stenosis and aortic incompetence Repeated periods of C H B under observation
27	57	0 2	R B B Bl	1 week after	C H B R B B Bl	Hypertensive heart failure No complaint of syncope
28	64	0 17	L B B Bl	5 days after	2 1 H B L B B Bl	Lt mammary pain for 2 weeks Frequent faintness Not unconscious P rate noticed to drop by half on several occasions Cardiac infarction is not excluded
29	56	0 19	L B B Bl	7 weeks after	C H B R B B Bl	For 3 weeks before C H B found in EC præcordial pains at rest and with exertion lasting up to 20 minutes Cardiac infarction
30	58	0 2	No B B Bl	16 days before and 9 days after	C H B	Referred from Venereal Clinic Angina pectoris Treated syphilis Cardiac infarction not excluded, although unlikely
31	82	0 18	R B B Bl (newer type)	15 weeks after	C H B R B B Bl	Hypertensive heart failure in C H B Regained N R after treatment by rest and digitalis

to be stressed concerning A-V conduction time is that the longest interval in the three limb leads should be taken as the true reading for that cardiogram   This seemed to be found most commonly in lead II, although other observers have considered lead III to be the most reliable single lead for the measurement of the time intervals (White, Leach, and Foote, 1941)   In no cases studied in these three groups was there any evidence of ventricular tachycardia or similar arrhythmia, and it is probable that, as usual in paroxysmal heart block, the Stokes-Adams attacks could be classified in Group I of Parkinson, Papp, and Evans (1941) namely, ventricular standstill alone

SELECTED CASE HISTORIES

Case 13   Female, aged 57, with hypertension   She had fallen unconscious on two occasions in the three months before she was seen in C H B   Similar attacks recurred while she was under observation during the next four months   In one cardiogram, normal rhythm with a P-R interval of 0 2 sec was seen in leads II and III although there was 2 1 A-V block in lead 1 (Fig 1)   On other occasions C H B was recorded and there was L B B Bl in all tracings
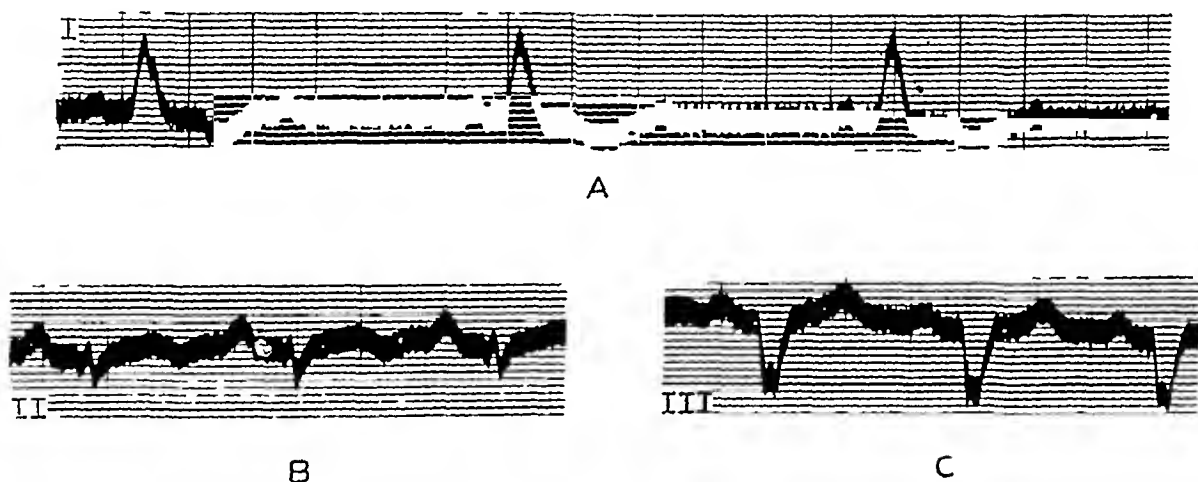
Fig 1 —*Case* 13   (A) Left bundle branch block with 2 1 A-V block in lead I   (B) and (C) normal sinus rhythm in leads II and III on the same occasion

Case 14   Male, aged 49   Referred from the Neurological Department, he had previously been suspected of having epilepsy   For 3½ years he had been troubled by very short attacks of faintness, and for 22 months he had been falling unconscious, sometimes hurting himself   An aura consisted of giddiness, but there was never tongue-biting or incontinence   No attacks were witnessed in hospital   His cardiogram showed R B B Bl and normal sinus rhythm with P-R 0 2 sec   Because of this normal P-R interval, Stokes-Adams disease was considered unlikely to be the cause of these faints which continued unchanged   Eight months later a cardiogram was obtained which showed C H B, and L B B Bl   (*N B* —Change of bundle branch block from left to right)

Case 17   Male, aged 72   He reported three isolated attacks of unconsciousness, 24, 18, and 4 months previously, but had suffered repeated faints during the two weeks prior to his admission to hospital   His first cardiogram portrayed C H B, and R B B Bl of the common type   Eight days later in normal rhythm his tracing contained a P-R interval of 0 18 sec   In the following month two further cardiograms were obtained with normal sinus rhythm and P-R intervals of 0 2 and 0 18 sec respectively
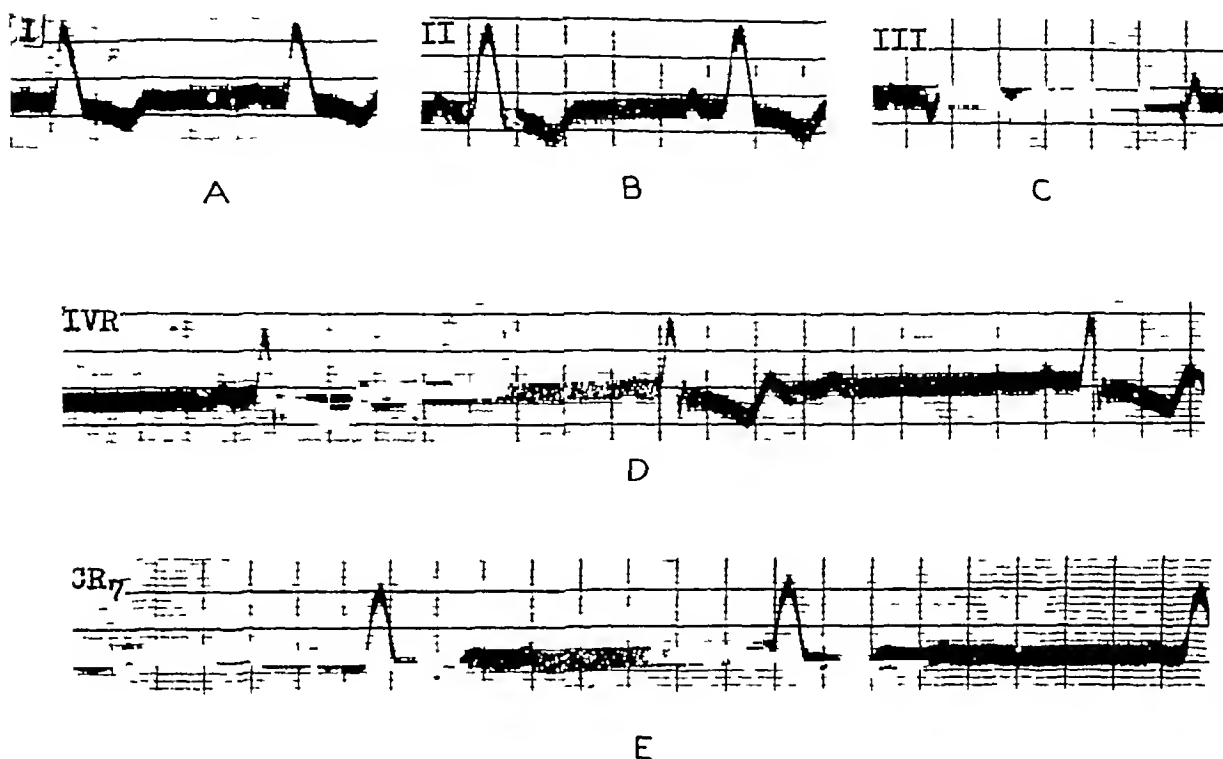
Fig 2 —Case 19   (A) (B), and (C)   Left bundle branch block with normal sinus rhythm and P-R interval
0 19 sec , in limb leads   (D) and (E)   A few minutes later 2   1 A-V dissociation in IVR and CR-

Case 19   Male, aged 51   He first complained of dyspnœa on exertion and fainting attacks
12 years before he attended the Cardiac Department   No syncope had occurred in the last
9 years until, in the last three weeks, these bouts had returned with sudden violence   His
pulse was regular at 44 to the minute and the blood pressure was 140/80   The limb leads of
the cardiogram showed normal sinus rhythm at 60 a minute, L B B Bl , and a P-R period of
0 19 sec (Fig 2)   When his chest leads were taken a few minutes later, however, there was
2   1 A-V block with a ventricular rate of 37   Eight months later there were C H B and
R B B Bl   (N B —Change of branch block)
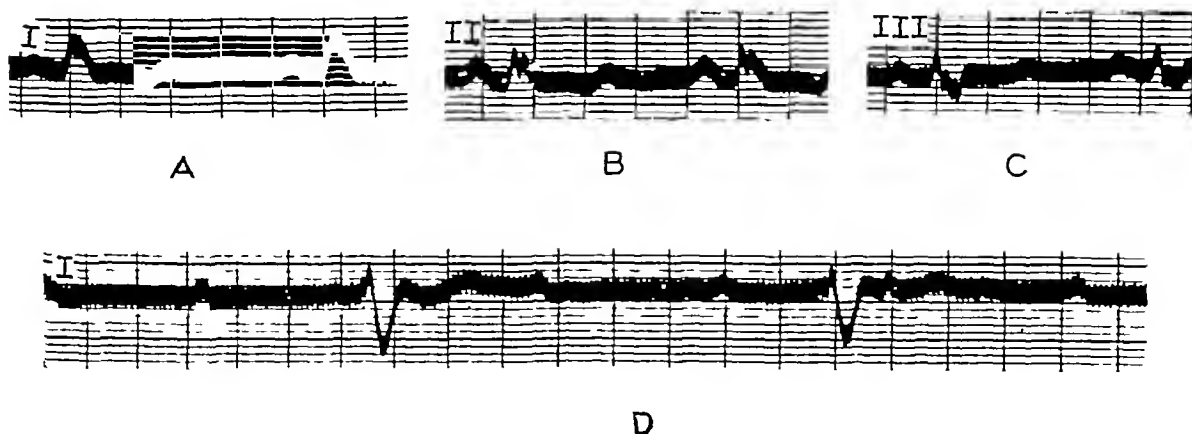
Fig 3 —Case 23   (A), (B), and (C)   Left bundle branch block normal sinus rhythm and P-R interval
0 18 sec   (D) Thirty-one months after   Complete heart block and right bundle branch block

Case 31　　Female, aged 82　　This patient had *C H B* and *R B B Bl* when she was first examined　　The diagnosis of hypertensive heart failure was confirmed radiologically　　After treatment by rest and digitalis, she regained normal rhythm　　Fifteen weeks after the first cardiogram, the P–R period was 0 18 sec　with *R B B Bl*, and the hilar regions were clear of congestion on cardioscopy

RESULTS

Among the 13 cases with normal QRS complexes there were 3 (Cases 3, 8, and 30) whose electrocardiograms in normal sinus rhythm showed P–R periods measuring 0 2 sec　or less In the combined groups there were 18 cases with bundle branch block　　Thirteen of these, when in normal sinus rhythm, showed normal P–R periods　　If one disallowed those cases that were complicated by heart failure or by possible infarction, the percentage with normal

A　　　　　　　　　　　　　　B　　　　　　　　　　　　　　C

D
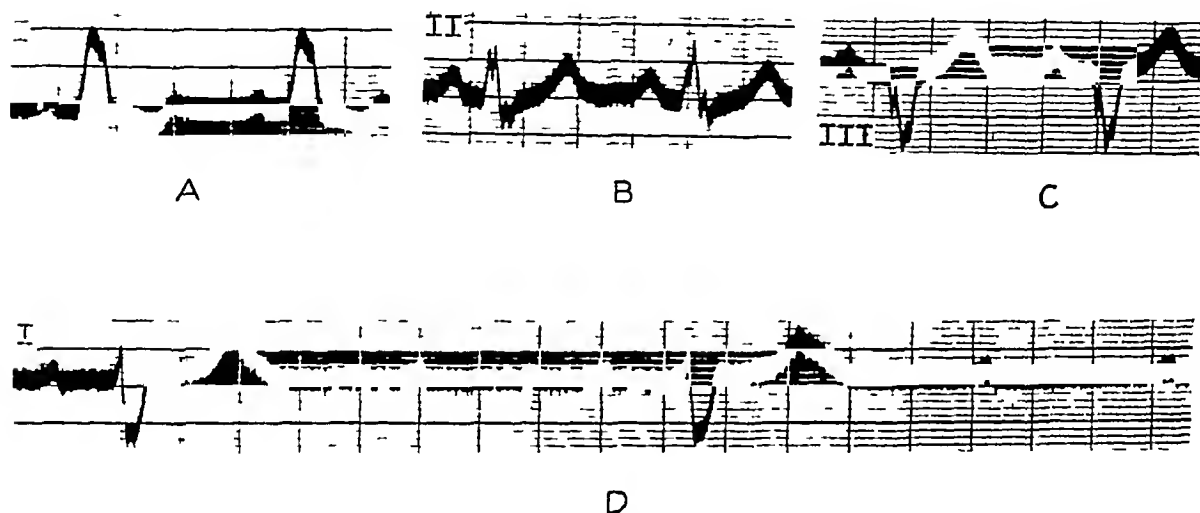
FIG 4　Case 29　(A), (B) and (C)　Left bundle branch block in normal sinus rhythm with P–R interval 0 19 sec , seven weeks after complete heart block with right bundle branch block (D)

A–V conduction time was the same　　Adding those with heart failure, but still excluding the patients who may have suffered infarction, one found that this figure was about the same It would therefore appear that the presence of bundle branch block increases the tendency to A–V dissociation in patients with normal P–R intervals, and that in cases of paroxysmal heart block, a prolonged P–R interval is less often recorded in the phase of normal sinus rhythm when bundle branch block is present than when it is absent from the cardiogram

DISCUSSION

In clinical medicine there has been a tendency to consider the bundle branches as separate from the main auriculo-ventricular stem, in spite of experimental facts that suggest that the conduction system should be studied as a whole　　First, the transmission of impulses in the bundle branches is included in the A–V conduction time　　Secondly, the effects of bilateral bundle branch lesions require consideration　　Wilson and Hermann (1921) remarked that lesions of the branches of the bundles of His had so far been shown to produce but two kinds of disturbances, namely complete bundle branch block and incomplete bundle branch block, the latter corresponding to delayed conduction in the main stem　　They concluded from experiments that when one branch of the bundle is interrupted, lesions of the remaining branch have the same effect as lesions in the main stem　　Scherf and Shookhoff (1925) by cutting one bundle branch and compressing the other between its upper and middle third, were able to

produce various degrees of A-V block, ranging from simple prolongation of the P–R period to marked second degree or transient complete block   Our knowledge today is well summarized by Dressler (1945)   A disturbance of conduction that involves equally both bundle branches, produces electrocardiographic changes indistinguishable from those caused by lesions of the main stem of the bundle   Interruption of conduction in both bundle branches brings on complete A-V dissociation, or, if there is an equal delay, as opposed to complete block, in both bundles, it is added to the A-V conduction time causing prolongation of the P–R period   As connecting pathways between the bundle branches and between the common trunk and the interventricular myocardium are found in many hearts, the A-V conduction time occasionally may be normal in spite of destruction of both branches   This has been termed " bilateral missed block " (Maheim, Winston, and Roesler, 1943)   From histological examinations of the conducting system in cases of intraventricular block, it is known that both bundle branches are usually involved (Maheim, 1931, Yater, Cornell, and Clayton, 1936 Yater, 1938)   It is also understood that depression of conduction in either one or both bundle branches may occur with little structural disease (Sigler, 1944)   Variations of conduction in the bundle branches are now recognized more frequently (Comeau, Hamilton, and White, 1938)   Variable ventricular complexes in heart block and their relation to bilateral bundle branch block were discussed by Bain (1944)   Mathewson (1913) who first described such complexes, thought that in his case the impulse was conducted alternately by each branch Cases of sinus rhythm with intraventricular block in which the type of ventricular complex varied, have been reported by many authors, reference to whom was made by Strauss and Langendorf (1943)   More recently alternating bundle branch block has been discussed by Alvarez *et al* (1944), and Dressler (1945) described two cases in which the P–R interval increased with changes from left to right intraventricular complexes   This variation in conductivity of the bundles, together with the facts mentioned, strongly support the belief that a sudden increase of impairment in both bundles, amounting to bilateral block, may cause auriculo-ventricular block

In the experience of Campbell (1943), the association of bundle branch block with latent heart block (prolonged P–R interval) was much more common than would be expected if it were a chance coincidence   In 1944 he commented on the closer association between bundle branch block and complete heart block, intraventricular lesions being present in nearly 30 per cent of his series of complete heart block   Although by themselves such associations prove nothing, they are to be expected if there is any truth in the theory of occasional A-V dissociation through bilateral bundle branch block

<p style="text-align:center">CONCLUSION</p>

The electrocardiograms of 31 patients over 40 years of age, with sometime A-V dissociation (2 to 1, or complete) were specially examined for the presence of bundle branch block, and for the length of the P–R period at a time when there was sinus rhythm   Bundle branch block was present in 18 and absent in the other 13 patients   In the 18 cases with bundle branch block, the P–R period was normal in 13, and long in 5   In the 13 cases without bundle branch block the P–R period was normal in 3, and long in 10

Thus, paroxysmal heart block is more likely to occur in patients with a normal P–R period if there is bundle branch block than if the QRS complexes are physiological   This observation is of some clinical importance in the diagnosis of Stokes-Adams disease when the cardiogram does not show A-V block

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THE FIRST HEART SOUND IN AURICULAR AND VENTRICULAR EXTRASYSTOLES

BY

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It is well known that the first heart sound of a premature beat may be of greater or lesser intensity than the first sound of the preceding or following normal beats (Cossio, 1944) An increased intensity of the extrasystolic first sound might be due to the onset of a premature ventricular beat coinciding with the auricular systole of sinus origin (Lewis, 1935), but this explanation could only apply to an extrasystole of ventricular type As Cossio and others (1943, 1944, 1945) have shown that an increased intensity of the first sound depends on the position and tension of the auriculo-ventricular valves at the onset of ventricular systole, it was decided to investigate the behaviour of the first sound in premature beats and to determine its clinical significance

Present Investigation

Simultaneous electrocardiographic and phonocardiographic records, with a camera speed of 75 mm a second, were obtained from 30 patients with extrasystoles First, the auricular or ventricular origin of the premature beats, and their situation in diastole, that is their degree of prematurity, were established, and also the time relation of the ventricular systole of the premature beat to the premature auricular systole in the case of auricular extrasystoles, and to the auricular systole of sinus origin in the case of ventricular extrasystoles Secondly, the intensity of the first sound of the premature beat was determined by phonocardiogram and compared with that of the preceding and following normal beats The time interval between the onset of ventricular systole and the first sound (onset of QRS to first sound) was determined both in the premature and the normal beats •

Of the 30 cases investigated, 16 proved to have auricular and 14 ventricular extrasystoles

Auricular Extrasystoles

In all but one of the 16 cases (Table I), the extrasystolic first sound was always louder than the first sound of the preceding and following normal beats The time interval between the onset of QRS and the reinforced extrasystolic first sound varied from 0 05 to 0 08 seconds, while in the case of normal beats or premature beats without reinforcement of the first sound, it was 0 03 to 0 05 seconds Thus in relation to QRS, the reinforced extrasystolic first sound occurred from 0 01 to 0 05 seconds, average 0 03 seconds, later than the first sound of normal beats

The increased intensity of the extrasystolic first sound and its corresponding delay bear a close relation to its degree of prematurity The greatest intensity and delay of the first sound was observed when the extrasystolic ventricular systole occurred some time after the T wave of the preceding cycle, that is in mid-diastole (Fig 1) In contrast, the first sound was less intense, even less than that of normal beats, when the extrasystolic ventricular systole occurred

TABLE I

PHONOCARDIOGRAPHIC AND ELECTROCARDIOGRAPHIC FINDINGS IN 16 CASES OF AURICULAR EXTRASYSTOLES

Case	Normal beat		Premature beat		First sound normal beat		First sound premature beat		Remarks
	R–R interval in seconds	P–R in seconds	R–R interval in seconds	P–R in seconds	Intensity	Onset of QRS to 1st sound	Intensity	On set of QRS to 1st sound	
1	0 69	0 18	0 57	0 20	+	0 03	+++	0 08	*
2	0 74	0 20	0 44	0 20	++	0 04	+++++	0 07	*
3	0 68	0 14	0 52	0 20	++	0 03	+++++	0 05	*
4	0 72	0 18	0 44	0 14	+++	0 04	++++	0 07	*
5	0 68	0 16	0 52	0 15	++		++++	0 06	*
6	0 88	0 12	0 46	0 14	+++	0 04	+++	0 05	*
			0 64	T+P		0 05	+++	0 07	
7	0 48	0 16	0 38	0 16	++		+++++	0 05	
8	0 48	0 16	0 42	T+P	++	0 05	+++++	0 07	Split extrasystolic first sound
			0 41	T+P		0 04	+++++	0 06	
9	0 70	0 14	0 48	0 08	++	0 05	+++++	0 06	(r) Accurate measurement not possible
10	1 08	0 20	0 52	0 08	+	(r)	+++++	( )	
			0 60	0 20			+++++	0 06	
			0 48	T+P			+++++	0 08	
11	0 88	0 16	0 51	0 18	++	0 04	+++++	0 06	Wandering pace-maker
			0 40	P+T			+++++	0 05	*
12	0 66	0 16	0 48	T+P	++++	0 03	+++++	0 07	
			0 52	0 18			+++++	0 06	
13	0 56	0 15	0 41	0 21	++++	0 04	+++++		*
14	0 75	0 14	0 56	0 16	+++	0 04	+++++		
15	0 92	0 14	0 56	0 16	+++	0 04	+++++		*
16	0 68	0 15	0 52	0 12		0 03	+++++		*

* Premature beat's first sound coincides with the rapid inflow phase
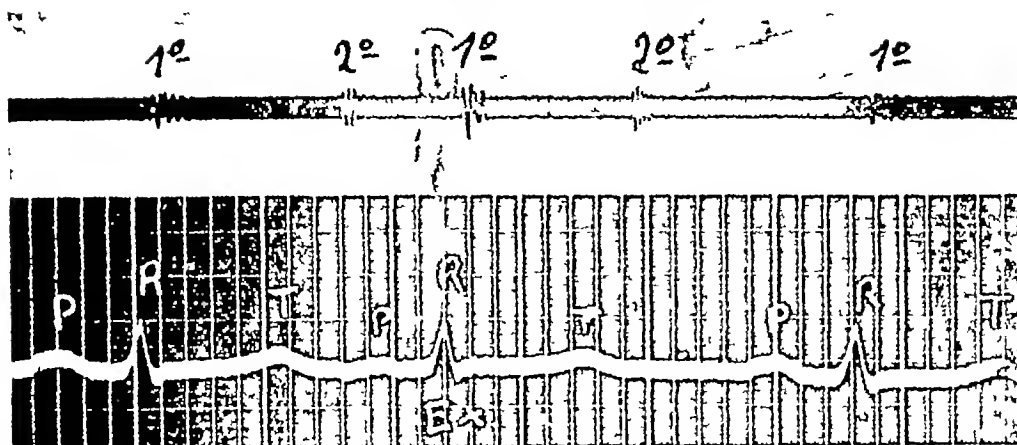
FIG 1 —Simultaneous phonocardiogram and electrocardiogram showing auricular premature beat falling in mid-diastole, the first sound is intensified and delayed
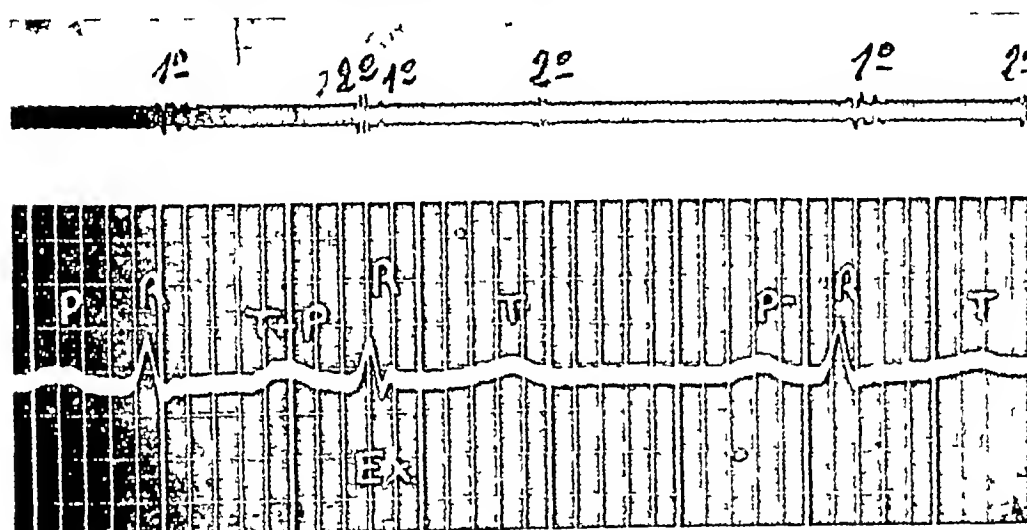
FIG 2 —Auricular premature beat occurring early in diastole, with a fainter first sound than that of normal beats
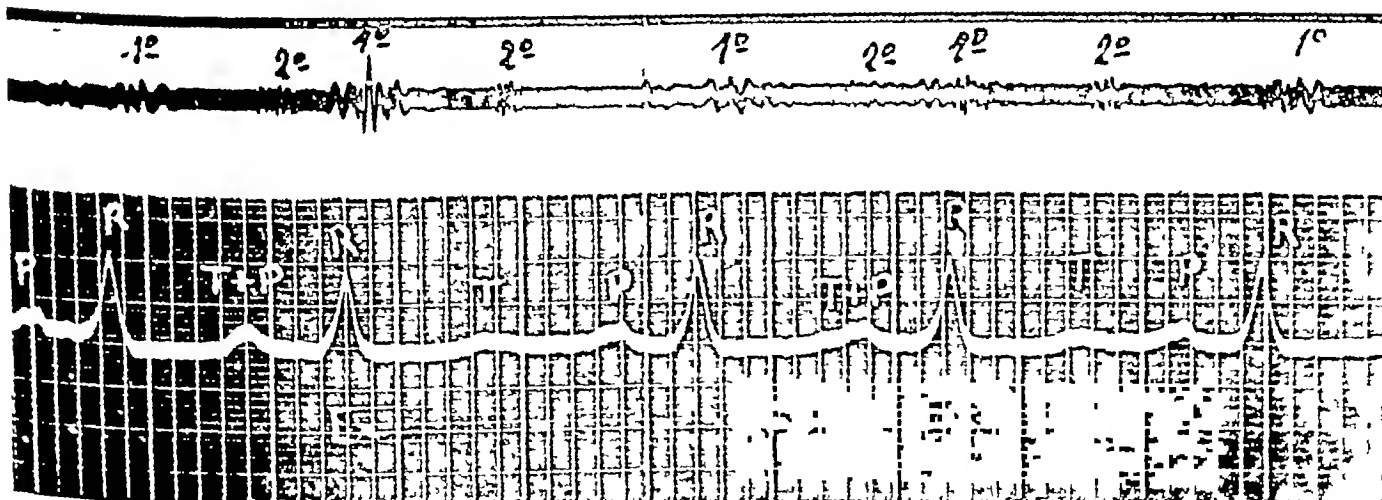
FIG 3 —Two auricular premature beats are shown the first occurring in mid-diastole has an intensified and delayed first sound the second falling later in diastole has a first sound of normal intensity and normal time relation to QRS

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TABLE II

PHONOCARDIOGRAPHIC AND ELECTROCARDIOGRAPHIC FINDINGS IN 14 CASES OF VENTRICULAR EXTRASYSTOLES

Case	Normal beat		Premature beat		First sound normal beat		First sound premature beat		Remarks
	R–R interval in secs	P–R in secs	R–R interval in secs	P–R in secs	Intensity	Onset of QRS to 1st sound	Intensity	Onset of QRS to 1st sound	
1	0 72	0 20	0 64 / 0 58	0 12 / 0 06	+	0·06	++ / +++	0 08 / 0 12	P at end of extrasystolic QRS
2	1 02	0 18	0 56 / 0 51		+++ / +++	0 06 / 0 05	++ / ++ (redpl)	0 12 / 0 08	P immediately after extrasystolic QRS Interpolated extrasystolic
3	0 88	0 12	0 40		++	0 05	++ (redpl)	0 11	P in ascending branch of extrasystolic QRS
4	0 70	0 14	0 52		± ++	0 05	+++	0 11	P immediately after extrasystolic QRS
5	0 88	0 16	0 44		++ (redpl)	0 04	++ (redpl)	0 09	P immediately after extrasystolic QRS
6	0 72	0 36	0 43		++	0 06	+++	0 12	P immediately before extrasystolic QRS
7	0 56	0 22	0 38 / 0 36	0·08	++	0 04	+++ (1) / +++ (2)	0 10 / 0 05 / 0 10	(1) Prolonged sound with preponderance of low-pitched components (2) Prolonged sound with both low-pitched and high-pitched components in equilibrum
8	1 02	0 20	0 56		++	0 06	+++	0 05 / 0 12 / 0 10	P immediately after extrasystolic QRS
9	1 20	0 16	0 56 / 0 60		+	0 05	++ r / ++ (1)	0 10 / 0 10	P immediately after extrasystolic QRS Interpolated prolonged sound (1)
10	0 88	0 18	0 64		++	0 06	+++	0 10	P in ascending branch of extrasystolic QRS
11	0 80	0 22	0 52		+	0 06	++	0 12	P immediately after extrasystolic QRS
12	0 86	0 16	0 64 / 0 44		++	0 05 / 0 44	++ / ++	0 06 / 0 08	P shortly after extrasystolic QRS P in ascending branch of extrasystolic QRS
13	0 60	0 16							
14	0 56	0 14	0 48 / 0 40		++	0 03	+++ / + (redpl)	0 07	P in ascending branch of extrasystolic QRS P shortly after extrasystolic QRS Reduplicated extrasystolic first sound

redpl = reduplicated sound

immediately after the T wave, that is in early diastole, or when it occurred very late in diastole (Fig 2 and 3) The A-V conduction time in premature beats with an increased first sound appeared to be longer than that of normal beats, but it could not always be determined exactly, as the extrasystolic P wave was sometimes fused with the preceding T wave

Ventricular Extrasystoles

In 14 cases investigated (Table II and Fig 4–7), the extrasystolic first sound was louder than the normal first sound in 9, of equal intensity in 1, of equal or less intensity in 1, and of less intensity in 3 cases The increased extrasystolic first sound was always delayed in comparison with the normal first sound The time interval between the onset of QRS and the increased extrasystolic first sound was from 0 08 to 0 12 seconds, average 0 10 seconds, while in the case of normal beats it was 0 03 to 0 06 seconds, average 0 05 seconds This delay
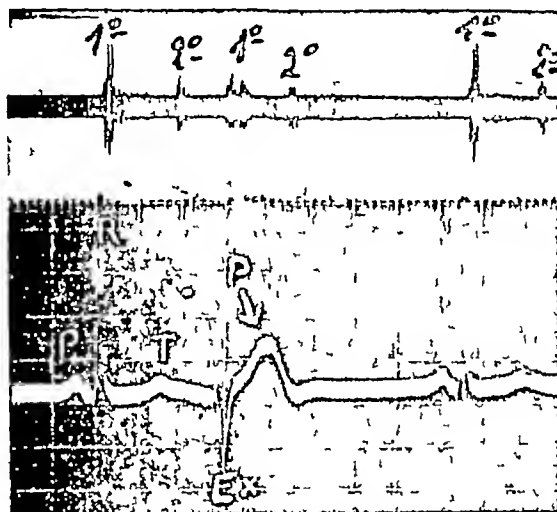
FIG 4 —Ventricular premature beat falling early in diastole, with faint and reduplicated first sound
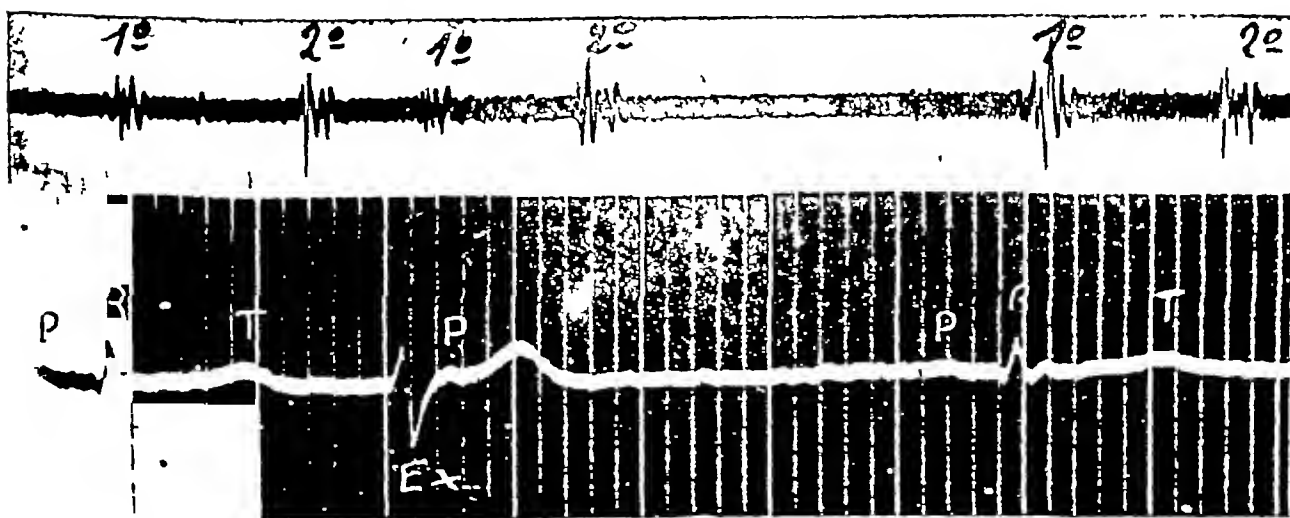
FIG 5 —Ventricular premature beat falling late in diastole, just before auricular systole, with a faint first sound

is especially evident in the case of the group of rapid vibrations of valvular origin belonging to the first sound, but not in the slower inaudible initial vibrations of muscular origin, which when magnified several times, were always found in the same position

The increased intensity and delay of the first sound in ventricular extrasystoles was related to their degree of prematurity and to their time relation with the normal auricular systole not followed by a ventricular response   Whenever the premature ventricular systole occurred so early that it coincided with the descending limb of the T wave of the preceding cycle (Fig 4), or fell later just in front of the next P wave of sinus origin (Fig 5), the extrasystolic first sound was less intense than that of normal beats   But whenever the premature ventricular systole fell just after the T wave, in mid-diastole (Fig 6) or just after the next normal P wave (Fig 7), the extrasystolic first sound was louder than that of normal beats   In 4 of the 14 cases, a split first sound was recorded in the premature beats, though not present in the normal beats
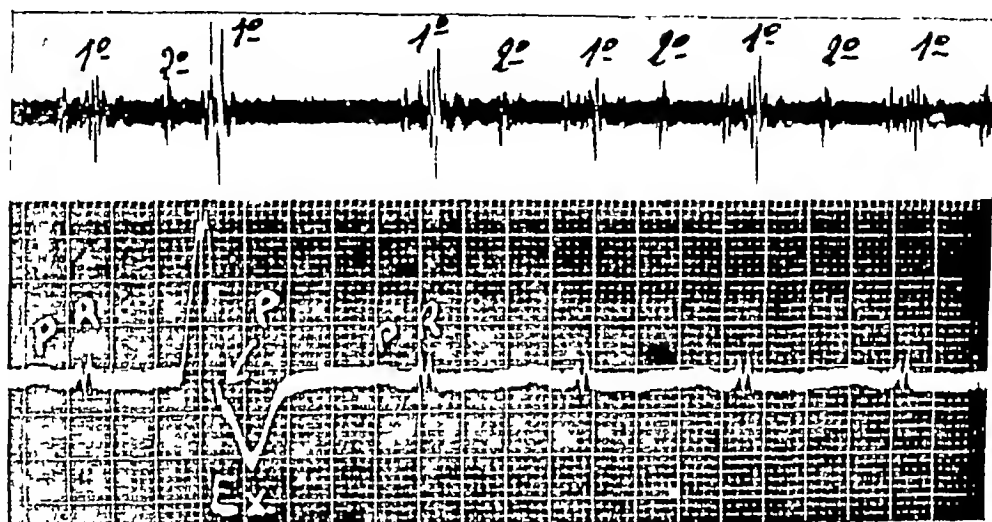
FIG 6 —Ventricular premature beat, falling, in mid-diastole, with an intensified first sound
Alternation of first sound of succeeding normal beats
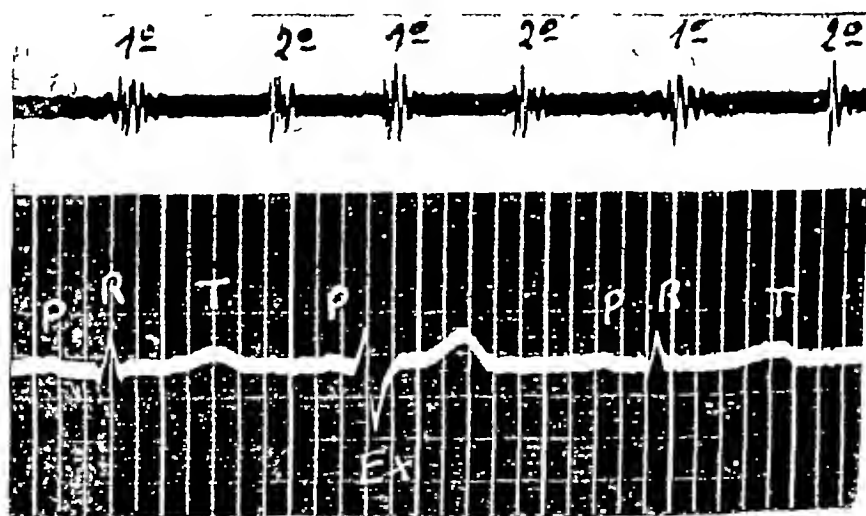
FIG 7 —-Ventricular premature beat falling late in diastole, just after auricular
systole, with a slightly intensified and delayed first sound

DISCUSSION

We conclude from our investigations that intensification of the first sound occurs as often in auricular as in ventricular extrasystoles, and, therefore, cannot serve to differentiate between them   A split first sound, on the other hand, is only produced in ventricular extrasystoles, though not in every case, and its presence suggests that an extrasystole is of ventricular origin Graphic records show that an intensified extrasystolic first sound is always appreciably delayed in relation to the onset of ventricular systole as recorded in the electrocardiogram   This relationship of the intensity of the first sound and the time of its occurrence has been called the *law of the first sound* (Cossio *et al*, 1943, 1944, 1945) and it has been attributed to the position and tension of the auriculo-ventricular valves at the onset of systole

During the cardiac cycle, the A-V valves perform a series of ascending and descending movements with corresponding increase and decrease in their tension   Dean (1936) has shown experimentally that, when blood flows from auricles to ventricles during the phase of rapid inflow, the A-V valves are forced downwards until the maximum opening is attained As the ventricles fill progressively during diastasis, the A-V valves gradually ascend until the occurrence of auricular systole, when they are again forced downwards, ascending again to a position of almost complete closure on the termination of auricular systole   Normally, the ventricular contraction finds the valves in this position, and their maximum stretch follows immediately, the vibration so produced, which Dock (1933) has shown to be the fundamental cause of the first sound, practically coincides with the onset of ventricular systole

But, if a ventricular contraction happens to occur at some other moment, for example, at the end of the phase of rapid inflow or during auricular systole, it will find the A-V valves in a much lower position, so that the distance travelled to reach the position of maximum stretch is longer, and consequently more time elapses between the onset of ventricular systole and the valvular vibration that gives rise to the first sound   When the valves have further to travel between the onset of ventricular contraction and the position of maximum stretch, their movement is accelerated, and consequently their vibration is increased, for the kinetic energy is the product of half the mass and the square of the velocity, and the velocity is the product of acceleration and time   This is precisely what has been shown to occur in premature beats, both auricular and ventricular, though more frequently in the former than the latter When the onset of ventricular systole in a premature beat coincides with an auricular systole of sinus origin, the first sound is intensified and delayed   Similarly, when the ventricular systole of either an auricular or ventricular premature beat falls at the end of or immediately after the phase of rapid inflow, the first sound is intensified and delayed

Thus there are two propitious moments for the production of the intensified and delayed first sound, at both of which the A-V valves are in their lowest position   When a premature beat falls before the end of rapid inflow, the A-V valves are also lowered, but in this case, owing to incomplete ventricular filling, the valves are insufficiently stretched to intensify the first sound

There are several reasons why the first sound is more often intensified and delayed in auricular than in ventricular extrasystoles   The first sound represents the summation of vibrations produced by the mitral and tricuspid valves   In auricular extrasystoles this normal summation is unaffected, but in ventricular extrasystoles a synchronism between the two ventricles prevents summation, and the first sound is split   Another reason is that auricular extrasystoles generally fall at a moment propitious for intensification of the first sound   Lastly, ventricular filling is more complete in auricular than in ventricular extrasystoles, because the former have the benefit of an auricular contraction which also contributes to lowering the A-V valves

SUMMARY

The characteristics of the first heart sound in auricular and ventricular premature beats

have been investigated by phonocardiographic records from 30 cases   In both varieties of extrasystole, the first sound was usually increased in intensity and delayed in relation to the onset of ventricular systole   In ventricular premature beats the first sound was sometimes split   The explanation of these findings is discussed in relation to the position and movements of the auriculo-ventricular valves

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THE PROGNOSIS OF PATENT DUCTUS ARTERIOSUS

BY

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Surgical intervention is becoming more frequent in patients with a patent ductus arteriosus At first only marked symptoms were accepted indications for surgery, but these are now becoming much more numerous This change has largely been due to the gradual decrease of the operative mortality and the dramatic cures effected in cases of bacterial endocarditis Gilchrist (1946) recommended operation on nearly all uncomplicated cases of patent ductus arteriosus between the ages of 7 and 10 years

The increased risk that the presence of a patent ductus involves is difficult to assess Surgeons see the more serious cases with symptoms or with infective endocarditis, and the prognosis without operation in such a series is gloomy Few physicians have published accounts of large numbers Maud Abbott's (1936) series based on post-mortem records paints too black a picture as patients with infective endocarditis and congestive heart failure tend to end their lives in hospital Shapiro and Keys (1941, 1943), Shapiro (1944), Wilson and Lubschez (1942), East (1945), and Gilchrist (1945) have all described series of cases but they do not mention how many were referred for symptoms and how many were symptomless This is important, as if a large number were referred because of symptoms there must be an excess of the more serious cases which naturally gravitate to hospital or the physician s consulting room

In the present series the diagnosis of uncomplicated patent ductus arteriosus was made only in the presence of a typical machinery murmur in the second left intercostal space with no evidence of any other abnormality on physical, cardiographic, and x-ray examination Forty-six cases have been collected for analysis and divided into two groups Group A numbers 30 and, save for one woman, aged 23, referred from an ante-natal clinic because of the presence of a machinery murmur, has been collected from a school cardiac clinic This must include almost every case of patent ductus arteriosus among the younger people of Bristol, whether they had symptoms or not Group B consists of 16 cases from areas outside Bristol referred in a few cases from school clinics but often because of symptoms It follows that Group A forms a representative sample of the condition while Group B approximates more nearly to the type of case generally reported

Sex Incidence Of the 60 cases of typical patent ductus arteriosus collected by Shapiro and Keys (1943) 14 were males and 46 females Steinberg, Grishman, and Sussman (1943) found that of 27 cases 11 were male and 16 female East (1945) had 4 males and 9 females, Gilchrist (1945) 13 males and 15 females, and Hunter (1945) found 4 males and 10 females The ratio of males to females varies considerably but in all series there is a preponderance of females varying from slight to very marked , In the present series 13 are males and 33 females These figures agree substantially with those of other authors

SYMPTOMS

Maud Abbott (1929) states that a fair proportion are dyspnœic, and that cyanosis, while usually absent, may be present on exertion Steinberg *et al* (1943) found 12 of 27 cases

complained of breathlessness   Gross (1939) found his were usually undeveloped and often breathless, but that only those with large ducts had symptoms   Gilchrist (1945) found his patients were often breathless without being aware of it until the patent ductus had been closed, and that in only 5 of 28 was there no limitation of physical capacity   Bullock, Jones, and Dolley (1939) found that only 2 of their 11 cases had no symptoms, all the others had palpitation and were easily tired

In the present series only 8 children have symptoms at present   Four are slightly breathless on exertion, 3 are easily tired, 5 become slightly blue on occasions, 2 suffer from frequent colds, and only 1 did not play games   In addition 2 children are subject to asthma   Three have more than one symptom   The 30 in Group A include 6 with symptoms, while the 12 surviving members of Group B contain 2 with symptoms   Five of Group B have had bacterial endocarditis and only 1 of these is alive now, this last child was cured by penicillin and is now symptom free   Thus, 7 of the 16 cases in Group B have at some time had symptoms attributable to a patent ductus arteriosus

PHYSICAL SIGNS

Cases have been described, without murmurs or with systolic murmurs only, that have been proved to have a patent ductus arteriosus post-mortem   Some of these descriptions are of doubtful accuracy as they were before the existence of the typical machinery murmur was recognized, but others are well authenticated   The question of absent murmurs is dealt with later   Descriptions of cases with systolic murmurs only are particularly common before 1910   Typical examples are by Gerhardt (1867), Wasastjerna (1874), Darier (1885), Thomson and Drummond (1900), Simmons (1906), Carpenter (1908), Goodman (1910), Motzfeldt (1913), Wessler and Bass (1913), Weiss (1931), Touroff and Vessell (1940), and Chapman and Robbins (1944)

Shapiro (1944) drew up the following list of the chief findings in cases of patent ductus arteriosus—the presence of a machinery murmur, a systolic thrill in the pulmonary area, an enlarged pulmonary artery, enlarged pulsating pulmonary vessels, a large heart, an increase of the pulse pressure, stunting of growth, absence of cyanosis and of clubbing of the fingers, a normal electrocardiogram, and the presence of heart disease from early childhood   He states that a thrill is usually present (53 of his 62 cases), but may be absent if the ductus arteriosus is small   Gross (1940) also says that a thrill is usually present but that the physical signs of patent ductus arteriosus are frequently not present until the age of 3 years

In the present series the above criteria have been used in diagnosis   A machinery murmur has been present in all, and all are over 3 years of age   Of the 46 cases 30 had a systolic thrill, 19 of the 30 in Group A had a thrill at some time, but in 3 it vanished with increasing age, in Group B, 11 had a thrill and in 1 it disappeared later   In no case did a thrill become evident if it had been absent earlier   The thrill may have disappeared because the chest wall grew thicker with age, but this does not seem likely as in 2 of the 4 cases examination at intervals of one year showed it to be present on the first and absent at the second occasion   These two lost their thrill by 5 and 6 years of age respectively   In a third case the interval was 4 years   It would seem more likely that some change took place in the volume or mechanics of the circulation

BLOOD PRESSURE

Bullock et al (1939) found that all but one of their 11 cases of uncomplicated patent ductus arteriosus had a high pulse pressure and a low diastolic pressure   Gross (1943) said the diastolic pressure was a measure of the leak and pointed out that among 48 cases, who survived operation for closure of a patent ductus, the diastolic blood pressure which had been low rose to normal after operation   Of their 22 cases, Shapiro and Keys (1941) found only 5 with a pulse pressure of less than 45 and the average was 59   Among normal people they

did not find any pulse pressure higher than 45   Shapiro (1944) said the pulse pressure may be normal if the ductus arteriosus is small   In his 60 cases (including the 22 cases just mentioned) he found the pulse pressure normal in 14, but it was increased in the remaining 46   Tubbs (1945) found the average diastolic pressure was 50–60 mm   Gilchrist (1945) in his series of 28 cases found the average diastolic pressure below the age of 10 years was 48, and the average systolic pressure 95, over the age of 11 years the average diastolic pressure was 53 mm   Judson and Nicholson (1914) found that the average diastolic pressure in normal children of 3 to 15 years ranged between 64 and 71 and the systolic pressure between 91 and 106, the pulse pressure being about 30 mm

Bohn (1938) measured the diastolic blood pressure of cases with a patent ductus arteriosus after exercise and found it fell to nearly zero   This fall has been substantiated by Shapiro and Keys (1941)

Of the 30 cases for whom blood pressure readings are available only 5 have a pulse pressure of less than 45 mm , this agrees with the findings of Shapiro and Keys (1941) quoted previously

TABLE I

THE BLOOD PRESSURE IN PATIENTS WITH A PATENT DUCTUS ARTERIOSUS AND THE EFFECT OF EXERCISE

Age		Number of cases	Average pulse pressure	Average diastolic pressure	Number with a diastolic pressure of 60 mm or below	Number of cases with a change of diastolic pressure after exercise		
						Fall	Rise	No change
Group A	15 years or below	10	53	66	3	3	0	3
	16 years or above	11	55	74	1	3	2	4
	Total	21	—	—	—	6	2	7
Group B	15 years or below	6	69	68	1	3	1	0
	16 years or above	3	58	72	0	0	0	1
	Total	9	—	—	—	3	1	1
Grand total		30	—	—	5	9	3	8

Five cases had diastolic blood pressures of 60 or below, this is contrary to the findings of Tubbs (1945) and Gilchrist (1945) and most of the blood pressure readings come into the range of normal as defined by Judson and Nicholson (1914)

The effect of exercise on the blood pressure is not so easy to obtain as has been suggested Children and even adults often refuse to exercise to the point of distress   In 3 the diastolic blood pressure rose after exercise (see Table I) and in no case did it fall to nearly zero   Of the 8 cases showing a fall in diastolic pressure the greatest drop was 20 mm , the lowest 5 mm , and the average 10 mm   The test is sometimes useful, but a rise in the diastolic pressure after exercise does not invalidate the diagnosis of a patent ductus arteriosus

THE ELECTROCARDIOGRAM

Brody and Randell (1935), Bullock et al (1940), Touroff and Vessell (1940) and Holmes 1945) have all reported cases of mild left axis deviation   Many other changes have been reported but similar changes in the cardiogram were found in normal children by Lincoln and Nicholson (1928) and by Perry (1931)   Gross (1940) pointed out that right axis deviation suggests the presence of some associated abnormality particularly pulmonary stenosis   Steinberg et al (1943), among their 27 cases had 4 with left and 8 with right axis deviation   Tubbs (1945) said slight axis deviation was occasionally present   Gilchrist (1945) found left axis

2A

deviation in 7 of his 13 cases all being below the age of 7 years   East (1945) found the cardio-gram normal in all his 13 reported cases   In none of these series are the criteria of normality laid down   The general opinion appears to be that apart from mild left axis deviation the electrocardiograms are normal in this condition

In the present series the axis deviation index as described by Paul White (1944) was measured   Cardiograms of 40 cases were available and only 2 cases showed axis deviation, there being one example of right and another of left deviation   No other abnormalities were present

X-RAY EXAMINATION

Post-mortem examinations have shown that the pulmonary artery, and either or both ventricles are frequently enlarged   Eppinger and Burwell (1940) X-rayed 9 cases and found the left ventricle was enlarged in 8, the pulmonary artery prominent in 8, and that pulmonary congestion was present in 9   Gross (1940) found the cardiothoracic ratio increased slightly, the pulmonary artery prominent and the lungs engorged   This was confirmed by Donovan et al (1943) who found that among 50 cases most hearts were enlarged and the lungs con-gested   Grier (1943), and Steinberg et al (1943) agreed   Shapiro (1944) in 62 cases found the heart enlarged in 40 and markedly enlarged in 4 of these   Gilchrist (1945) found 7 of his 27 cases did not have enlarged hearts on X-ray examination

In the present series the normal ratio of the transverse diameter of the heart to the trans-verse diameter of the chest is taken to be 0 45 in adults and 0 52 in children with a normal variation of 10 per cent   Satisfactory X-rays were available in 15, the bounds of normal were exceeded in only one and the ratio in this was 0 66   All 15 had prominent pulmonary arteries   The degree of pulmonary congestion was measured by assessing the heaviness of the shadows around the hilum, but the incidence cannot be compared accurately as the variations of the normal are assessed differently by each observer   Of the 30 patients with X-rays suit-able for examination, 15 showed congestion and the remainder were normal   In Group A, 8 of 20 cases showed congestion and in Group B, 7 of 10 cases are congested   This suggests that among an unbiased series of cases of patent ductus arteriosus (as opposed to a series containing many with symptoms) increased size of the heart and pulmonary congestion is less common than has so far been reported

No correlation between the presence of symptoms and the presence of pulmonary con-gestion was found (Table II)

TABLE II

THE INCIDENCE OF SYMPTOMS

	Number of cases with symptoms	Number of cases with no symptoms	Total
Pulmonary congestion present	4	11	15
Pulmonary congestion absent	2	13	15
Total	6	24	30

ABSENCE OF THE MACHINERY MURMUR

Luys (1855) in 1848 saw a woman of 52 years in whom physical examination revealed no murmur, post-mortem the ductus arteriosus was patent   Duroziez (1862, 1863) found a woman aged 40 years with early congestive heart failure in whose chest he could hear no cardiac murmurs   the ductus arteriosus was patent, post-mortem   Foulis (1884) had a woman patient of 22 years with the typical basal systolic and diastolic murmurs in whom the murmur disappeared 25 days before she died of bacterial endocarditis   Balfour (1898) described a

cyanosed and breathless woman, who had a loud systolic murmur over the heart with a thrill over the second and third intercostal spaces to the left of the sternum, fifteen years later the murmur and thrill had disappeared proof that this was a case of patent ductus arteriosus is hardly complete Gaylor (1918) described a woman first seen by Babcock in 1898, who had a machinery murmur and thrill at the base of the heart, as the years went by the murmur vanished and post-mortem there was a saccular aneurysm of the aorta and a patent ductus arteriosus

Gross (1939) said that in some children the ductus closed spontaneously and the diastolic element in the machinery murmur was lost Shapiro and Keys (1943) described a woman of 46 years in heart failure over whose præcordium they could hear no murmur but post-mortem the ductus was patent In the same paper they mention having seen 2 cases with the typical murmur that later vanished Gilchrist (1945) described a boy aged 5 years with the typical murmur which had vanished at 6 years When first seen his X-ray picture was characteristic of a patent ductus arteriosus but 18 months later it was normal Jager (1940) and Gibb (1941) each described a woman, aged 55 and 51 respectively, with subacute bacterial endocarditis with no abnormal murmurs post-mortem, the ductus was blocked in each case by vegetations

The explanation of these findings appears to vary Some may be explained by blocking of the ductus by vegetations in cases with infective endocarditis The X-ray changes in Gilchrist's case appear to be due to actual closure of the duct Other cases appear to be explained by the onset of heart failure Some may be explained by thickening of the chest wall, emphysema, increase of adipose tissue, change in hæmodynamics, or in the position of the ductus relative to the chest wall Gebauer (1943) found at operation that the size of the ductus and the amount of blood going through it varied as the intensity of the physical signs

In the series under examination, 2 had well established machinery murmurs that have now vanished neither case ever had a thrill The first had a typical murmur on repeated examination between the ages of 8 and 13 years, a faint systolic murmur only could be heard at 15 years, and later at 21 years, and now at 25 years no murmur is audible The second case was first diagnosed at the age of 10 years, a soft basal systolic murmur was heard at 24, and now 3 years later no murmur can be heard An X-ray of the first case at 9 years revealed slight pulmonary congestion and the cardio-thoracic ratio was $102/212=0 48$ The pulmonary artery index, being the distance of the junction of the superior vena cava and the right auricle from the summit of the pulmonary arc, as described by Evans (1943), was 5 2 cm At the age of 25, X-rays still show some pulmonary congestion, the cardio-thoracic ration is $117/263=0 44$, and the pulmonary artery index is 7 1 cm Evans (1943) found the index above 7 0 cm in only 2 of 52 normal cases The heart did not become smaller as described by Humphreys (1942) and others after operation These findings suggest that the ductus is probably still patent In the second case X-rays are not available The blood pressure of the first case is 120/80, which does not indicate a leak but does not disprove the diagnosis The second case has a blood pressure of 120/60, which is unaltered by exercise Gross (1940) stated that closing the ductus by surgery causes the diastolic blood pressure to rise to normal This reading, therefore, suggests that the ductus is still patent Neither patient is obese or emphysematous No definite conclusions can be drawn, but the findings suggest that in both the ductus arteriosus is still patent

PHYSIQUE

Abbott (1929) and Gross (1940) found their cases of patent ductus were usually of poor physique In his 62 cases Shapiro (1944) found 32 were normally developed, 23 undersized, and 6 were obese Gilchrist (1945) in 13 children found the physique above average in 2, average in 7, and below average in 4

The height and weight of the present series has been compared with those of healthy children from the same area The controls were chosen at random from schools scattered all over

TABLE III
A Comparison of the Heights and Weights of Children having a Patent Ductus Arteriosus with Normal Controls

	Cases of patent ductus arteriosus			Normal Bristol children		Difference of case from controls	
Group	Age in years and sex	Height in cm	Weight in kg	Mean height in cm	Mean weight in kg	Height in cm.	Weight in kg
A	3 F	106 0	14 5	94 4	15 4	+11 6	−0 9
A	3 F	98·0	14 1	94 4	15 4	+3 6	−1 3
A	4 F	116 0	17 7	103 5	16 5	+12 5	+1 2
A	4 F	109 5	15 9	103 5	16 5	+6 0	−0·6
A	6 F	111 0	20 5	117 4	21 9	−6 4	−1 4
A	8 M	131 5	25 0	128 5	26 7	+3 0	−1 7
A	9 F	—	27 3	—	29 0	—	−1 7
A	9 F	130 5	25 0	133 1	29 0	−2 6	−4 0
A	10 F	—	30 9	—	31 6	—	−0 7
A	12 F	—	27 3	—	40 4	—	−13 1
A	12 M	—	33 2	—	37 5	—	−4 3
A	13 M	—	29 1	—	45 0	—	−15 9
A	13 F	—	28 2	—	43 4	—	−15 2
A	15 F	—	50 0	—	52 5	—	−2 5
A	15 M	178 0	56 4	169 5	57 2	+8 5	−0·8
A	16 F	160 0	57 7	165 9	55 4	−5 9	+2 3
A	17 F	170 0	41 8	169 3	58 7	+0 7	−16 9
B	9 M	134 0	24 5	130 5	28 5	+3 3	−4 0
B	10 F	127 5	20 5	137 5	31 6	−10·0	−11 1
B	10 F	147·0	47 3	137 5	31 6	+9 5	+15 7
B	11 F	142 0	25 9	142 7	35 4	−1 8	−9 5
B	11 F	—	38 2	—	35 4	—	+2 8
B	14 M	156 0	42 3	166 2	50 0	−10 2	−7 7
B	17 F	—	54 5	—	58 7	—	−4 2

Bristol (Table III)　For each year of age from 3 to 15, 50 children of each sex were taken and their height and weight measured　For children of 16 and 17 years only 26 and 10 controls were obtained　The figures for adults are compared with the figures for males and females aged 18, 20, and 25 years given by Cruickshank (1946) (Table IV)　For these no statistical analysis has been attempted as there is no adequate series of controls

The weights and heights of Group A have been analysed statistically because it is believed this group gives a true picture of the condition　The results have not been compared with Group B as there are not enough cases in this group with adequate data

Weights are available for 17 children in Group A and 15 of these children were below the mean weight of control children of the same age and sex　An analysis of variance was made to determine the significance of the difference between the weights of the children in Group A and the corresponding normal children, i e of the same sex and age　It was found that on comparing the 4 abnormal males with the 4 classes of normal males of the same age the significance of the lesser weight in the Group A cases was expressed by $P< 05$, i e was significant to the usual agreed 5 per cent level　In the case of the 13 females in Group A the significance was overwhelming, being expressed by $P< 001$

Heights are available for 10 children in Group A　Seven cases were above average height for their age and sex, while 3 were below the average　A similar analysis as for weights was made　In the two males the difference in height from the normal was not significant　In the 8 females the significance was expressed by $P< 05$, i e the Group A cases are taller than the normals

Prognosis

Abbott (1936) found that of 92 uncomplicated cases of patent ductus examined post-mortem 43 per cent died of heart failure and 30 per cent of subacute bacterial endocarditis　Among

TABLE IV

A COMPARISON OF ADULTS HAVING A PATENT DUCTUS ARTERIOSUS WITH NORMAL CONTROLS

	Cases of patent ductus arteriosus			Normal adults (from Cruickshank)		Difference of case from normal	
Group	Age and sex	Height in cm	Weight in kg	Height in cm	Weight in kg	Height in cm	Weight in kg
A	20 F	160 0	58 6	167 7	57 7	−7 7	−0 9
A	22 F	162 5	58 6	167 7	57 7	−5 2	−0 9
A	23 F	162 5	52 7	167 7	57 7	−5 2	-5 0
A	25 F	172 9	55 9	167 7	59 1	+5 2	−3 2
A	25 M	175 4	62 3	175 4	63 6	0	−1 3
A	25 F	152 2	42 3	167 7	59 1	−15 5	−16 8
A	27 M	167 7	59 1	175 4	70 0	−7 7	−10 9
A	27 M	172 9	65 9	175 4	70 0	−2 5	−4 1
A	31 F	162 5	50 0	167 7	59 1	−5 2	−9 1
B	33 F	160 0	45 9	167 7	59 1	−7 7	−13 2

her 73 cases over 3 years of age 16 per cent died of bacterial endocarditis and 32 per cent of heart failure   In 60 collected cases Shapiro and Keys (1943) found the average age at death of men was 39 years and of women 35 years, i e 23 and 28 years respectively less than the normal expectation   40 per cent died of bacterial endocarditis and 30 per cent of congestive heart failure   Sellors (1945) is even more gloomy and says the average expectation of life is 20 to 25 years   Wilson and Lubschez (1942) followed 38 cases for 20 years and in that time saw no deaths from bacterial endocarditis or congestive heart failure

In Group A, 29 of the 30 cases were seen before the age of 15 years the one exception was 23 years old when first seen and had been referred from an ante-natal clinic   At present the youngest person in the series is nearly 4 years old and the oldest 31 years   These cases have been followed for an average of more than 8 years and the average age when last seen was over 16 years   Of the cases in Group B, 9 were first seen before 15 years and 7 at a later age The youngest in this series is now 7 and the oldest 47 years   These cases have been followed for an average of 8 years   Of these 16 cases 12 are still alive and their average age is 19 years For the length of time the cases have been followed see Table V

TABLE V

THE LENGTH OF FOLLOW UP OF CASES OF PATENT DUCTUS ARTEPIOSUS

Time followed in years	Group A	Group B
0–5	9	4
5–10	7	4
10–15	6	2
15–20	7	0
20–	0	1

During the period under observation none of the Group A cases died or developed bacterial endocarditis or congestive heart failure   Among the 16 in Group B 1 case was first seen after recovery from bacterial endocarditis and 4 died of this disease, 1 of these 4 developed bacterial endocarditis and was treated with penicillin with apparent success although the blood sedimentation rate remained high   She returned home, but two months later suddenly developed fits and died the same night, presumably from a cerebral embolism due to a still active bacterial endocarditis

The incidence of bacterial endocarditis (5 cases out of 16) in Group B is high because several were referred to hospital because of its presence, and this same reason must explain the high

incidence of bacterial endocarditis in published figures The absence of such cases in Group A is striking and suggests that the frequency of bacterial endocarditis among all cases of patent ductus arteriosus must be lower than has so far been accepted The true incidence must lie between that in the two Groups, but much nearer to that of Group A The absence of congestive heart failure is not so significant as only a few of the cases have reached an age at which such a complication is likely

The Indications for Surgery

Hubbard, Emerson, and Green (1939) gave retardation of growth, signs of aortic regurgitation, and cardiac insufficiency as the indications for surgery Gross (1939) after 50 operations gave as his criteria, poor physique, cardiac embarrassment, bacterial endocarditis, and prevention of bacterial endocarditis Marvin (1941), Burch (1944), and Tubbs (1945) gave almost the same criteria

Gross (1940) said that operation caused the physical signs to vanish, the diastolic blood pressure to rise, the activity of the heart to diminish, the weight to increase, the heart size to decrease, and symptoms of heart failure to disappear Donovan *et al* (1943) found on X-ray that the heart size diminished only slightly, if at all, after operation Hunter (1945) had 12 cases all of which lost their breathlessness and became mentally brighter after operation Gilchrist (1945) found diminished lung vascularity and reduction in size of the heart in 14 patients who survived operation

Gross (1943) had 2 deaths in 50 operations Shapiro (1943) collected 104 reported cases treated surgically, none of which had bacterial endocarditis and found 9 deaths, presumably some of these were taken from Gross's records mentioned above Gilchrist (1945) had 16 cases operated on with 2 deaths

The absence of bacterial endocarditis in Group A suggests very strongly that it is much less common than has been described Most cases lead a normal healthy life On the other hand many are below average weight Bacterial endocarditis has become much less dangerous since the discovery of penicillin and the facts published in this paper suggest that operation with its grave risks hardly seems justified merely for the prevention of the possibility of infection However, cases cured of bacterial endocarditis appear to be proper subjects for operation as they are probably more liable to, or more exposed to infection The risks of dental extraction or operation on infected tonsils are great but they can probably be almost obviated by cover with penicillin The operative mortality is still high—possibly as high as, or higher than, the risk of bacterial endocarditis or congestive heart failure

This investigation suggests that at present operation should only be undertaken in a limited number of cases The indications for surgery would appear to be bacterial endocarditis, recovered bacterial endocarditis, cardiac embarrassment, or poor physique

A similar series of cases will need watching for at least 30 years before a complete answer can be given It would be very worth while if the numbers were large

Summary

A series of 46 cases of patent ductus arteriosus is described, particular attention being paid to 30 cases referred from a school cardiac clinic as these form a representative sample of the condition

Females predominate over males by more than two to one

Symptoms are few and rarely serious

In two cases the classical murmur disappeared without other evidence that the ductus arteriosus had closed Præcordial thrills sometimes vanish with increasing age The diastolic blood pressure is usually normal, in only a limited number of cases does it fall after exercise The electrocardiogram is normal

Pulmonary congestion is not so common as has been reported The average body weight is

significantly below normal Bacterial endocarditis did not develop among the 30 cases referred from the school cardiac clinic

Fewer cases should be operated on and the suggested indications for surgery are given

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CARDIAC CATHETERIZATION
IN CASES OF PATENT INTERAURICULAR SEPTUM, PRIMARY PULMONARY HYPERTENSION, FALLOT'S TETRALOGY, AND PULMONARY STENOSIS

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The clinical and radiological findings in auricular and ventricular septal defects are well known In many cases, however, the diagnosis may remain uncertain without pathological examination The development of the technique of cardiac catheterization as a simple and safe procedure indicated a method for the detection of intracardiac shunts, and a number of reports on the use of the method have already been published (Brannon, Weens, and Warren, 1945, Dexter *et al*, 1946, and Johnson, Wollin, and Ross, 1947) Not only can interauricular and interventricular shunts be demonstrated, but the amount of blood shunted and the pressure in the chambers of the right heart may be measured In certain cases the demonstration that no shunt exists may be helpful in diagnosis This paper reports data in a number of cases that were suspected on clinical grounds of having intracardiac shunts

METHODS

The technique of cardiac catheterization and analysis of blood samples were similar to those previously published (McMichael and Sharpey-Schafer, 1944) Arterial samples were obtained from the brachial or femoral arteries Average normal values are given in Fig 1 The following procedure may be found convenient

(1) A preliminary arterial sample indicates whether a right to left shunt has to be considered We have often found it difficult to judge clinically whether cyanosis resulted from a diminished arterial oxygen saturation or a diminished peripheral flow

(2) The catheter is passed into the right ventricle In the absence of conditions causing increased cardiac output the existence of a left to right intracardiac shunt may be suspected if the sampled blood from this position appears bright red like arterial blood, and on analysis is shown to have a high oxygen content

(3) The catheter is then withdrawn through the tricuspid valves into the right auricle and further samples taken Brannon, Weens, and Warren (1945) who published data on four cases by similar methods, calculated the magnitude of the left to right shunt through an auricular septal defect from the gas content of auricular blood and the mean gas content of the S V C and I V C samples With interatrial shunts auricular samples may not be completely mixed, and right ventricular samples are to be preferred if it is desired to make such calculations

(4) Samples may then be obtained from the superior vena cava and, if possible, from the inferior vena cava

In cases of right to left shunt the procedure should be carried out as quickly as possible with particular care to avoid clot formation on the tip of the catheter by a continuous drip

of heparinized saline, since there is a possibility of paradoxical embolism   Preliminary administration of heparin to the patient might be considered to lessen this risk   In children the investigation may be conveniently carried out under a basal anæsthetic
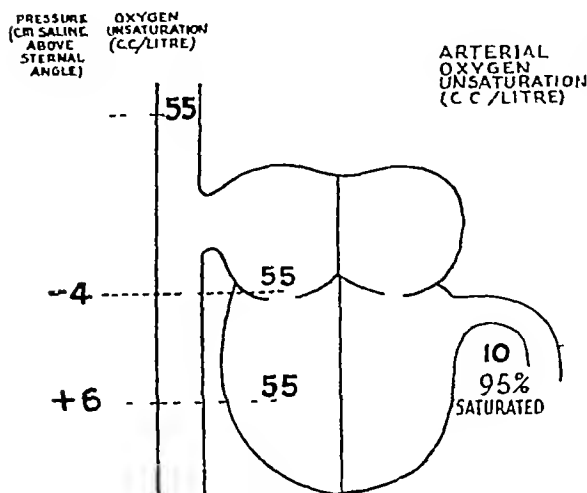
FIG 1 —Average oxygen unsaturation levels and mean right auricular and ventricular pressure measurements in normal supine subjects
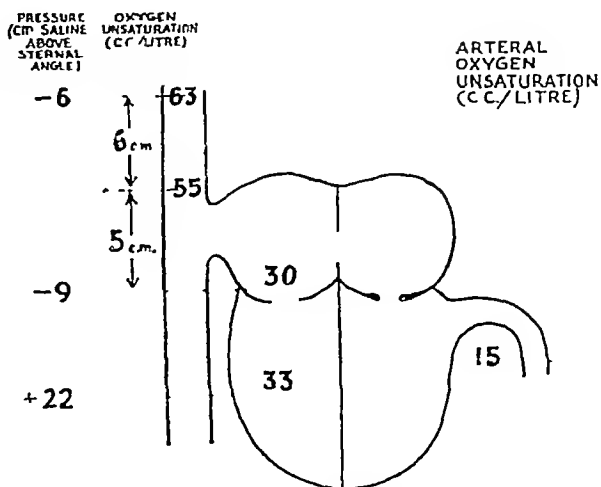
FIG 2 —Case 1   Data obtained by cardiac catheterization

CASE REPORTS

Case 1   A male, aged 57, was admitted complaining of loss of weight for two years and of bulky fatty stools for six months   An exploratory laparotomy had been performed elsewhere and a carcinoma of the head of the pancreas had been found   Slight dyspnœa on moderate exertion had been present for many years   There was no history of rheumatic fever   On examination there was no dyspnœa, cyanosis, or clubbing   The jugular venous pressure was normal   The blood pressure was 135/75 and the pulse regular at about 80 beats a minute   The heart was moderately enlarged and a systolic thrill and murmur were present, which were maximal at the apex   The hæmoglobin was 78 per cent   A cardiogram was not taken   Chest X-ray (Fig 4, see p 295) showed considerable enlargement of the pulmonary arteries, which pulsated strongly   The right ventricle and auricle were enlarged and the left auricle was not enlarged   The aortic knuckle was small   Total pancreatectomy was performed but the patient succumbed to post-operative complications

Necropsy   The heart weight was 490 g   The pulmonary arteries were greatly enlarged   The right ventricle was thickened and dilated and the left ventricle was normal   The right auricle was enlarged and there was an interatrial septal defect (Fig 3, see p 294)   The left auricle was normal in size   The mitral valve admitted two fingers and showed slight thickening of the free margins of the cusps

Comment   The clinical findings suggested patent interauricular septum with possibly mitral incompetence   While catheterization (Fig 2) clearly demonstrated the presence of a left to right interatrial shunt, the low normal right auricular pressure did not indicate any significant degree of mitral incompetence   Although the systolic thrill and murmur may have resulted from the slight thickening of the free margins of the mitral cusps, demonstrated post-mortem, they may also have been due to relative stenosis in the outflow tract from the right ventricle, in which chamber the mean pressure was considerably increased   During the prolonged and extensive operation for removal of the pancreas in this case, every effort was made to maintain right auricular pressure at or above the normal level by blood transfusion

2B

Fig 3 —Case 1   Heart viewed from the left side to show auricular
septal defect and slightly thickened mitral valve

At one time right auricular pressure was as high as 7 5 cm above the sternal angle, yet analysis of an arterial sample showed that there was no reversal of the shunt which remained from left to right auricle

Case 2   A man, aged 20, came to hospital for treatment of acne   He had attended a special school until the age of 6, but there was no history of rheumatism   He played football and did not complain of breathlessness   The jugular venous pressure was not raised and no œdema was present   The blood pressure was 140/85   Auricular fibrillation was present, the apex rate being 120   Systolic and low-pitched diastolic murmurs were heard at the apex The hæmoglobin was 94 per cent.   An electrocardiogram showed auricular fibrillation, right axis shift, and slight depression of S–T III   Chest X-ray revealed a small aortic knuckle, enlargement of the pulmonary arteries, and no enlargement of the left auricle (Fig 5, see p 295)

Comment   A case of patent interauricular septum   The data (Fig 6) showed that the shunt was from left to right   The diastolic murmur suggested that mitral stenosis may also have been present

FIG 5 —Case 2   Patent interauricular septum and mitral stenosis

FIG 4 —Case 1   Patent interauricular septum

Case 3   A woman, aged 41, had been diagnosed as suffering from congenital heart disease as a child   She had had no cardiac symptoms until the age of 39, but during the three months preceding admission to hospital, dyspnœa had been increasing and there had been swelling of the ankles   The jugular venous pressure was raised to 6 cm above the sternal angle, the liver was enlarged, and œdema was present   The blood pressure was 210/110   The heart rate was 80, with sinus rhythm   A systolic thrill and loud harsh systolic murmur were present, maximal in the third left interspace and conducted to the apex, and a short diastolic murmur was occasionally heard   The hæmoglobin was 89 per cent   The cardiogram showed no axis shift   There was slight depression of S–T in leads II and III, but all the T waves were upright   X-ray showed enlargement of both right and left ventricles, and moderate enlargement of the left auricle (Fig 8, see p 297)   The pulmonary arteries were also enlarged

Post-mo tem examination confirmed the diagnosis of patent interauricular septum   The right ventricle was dilated and hypertrophied and there was moderate hypertrophy of the left ventricle   The mitral valve showed some small vegetations   There was cylindrical dilatation of the pulmonary arteries

Comment   The data showed that the shunt was from left to right (Fig 7), although right auricular pressure was considerably increased above normal
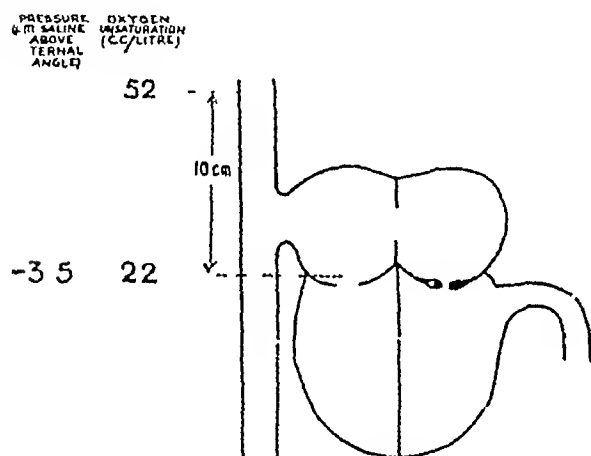
FIG 6 —Case 2   Data obtained by cardiac catheterization
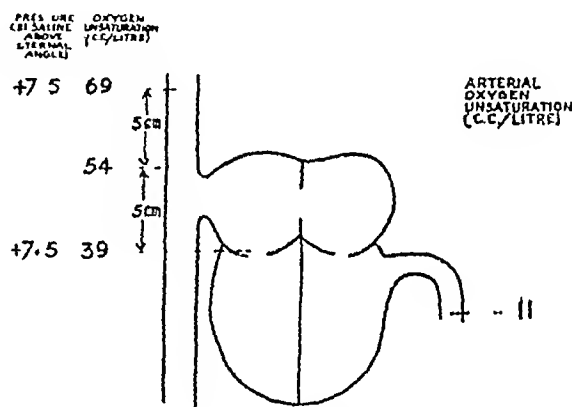
FIG 7 —Case 3   Data obtained by cardiac catheterization

Case 4   A woman, aged 40, gave a history of effort dyspnœa for 3–4 years and of attacks of nocturnal dyspnœa for 2 years   She had had rheumatic fever at the age of 11 years   The jugular venous pressure was not raised and there was no œdema   The blood pressure was 125/90   The heart rate was 108, with sinus rhythm   A harsh systolic murmur was heard over the lower part of the left side of the sternum, and the pulmonary second sound was increased   The hæmoglobin was 108 per cent   A cardiogram showed sinus rhythm, right axis shift and S–T II and S–T III depression   Chest X-ray showed enlargement of the right ventricle and of the pulmonary arteries (Fig 9, see p 297)   The left auricle was not enlarged

Comment   A case of patent interauricular septum   The data (Fig 10) showed that the shunt was from the left to the right

Case 5   A man, aged 31, had had two attacks of rheumatic fever 11 and 8 years previously He complained of slight effort dyspnœa for 1 year   The jugular venous pressure was slightly raised   No œdema was present   The blood pressure was 105/70, the heart rate 70, and the rhythm regular   A systolic murmur was present at the apex and the pulmonary second sound was accentuated   The hæmoglobin was 118 per cent   A cardiogram showed right axis

Fig 9—Case 4   Patent interauricular septum

Fig 8—Case 3   Patent interauricular septum

shift with S–T III depression   X-ray examination showed enlargement of right and left ventricles with prominence of the conus   the left auricle was not enlarged and the aortic shadow small (Fig 12, see p 299)

Comment   The difference in oxygen content between superior vena caval and right auricular blood indicated a left to right auricular shunt (Fig 11)   The lower unsaturation figure obtained in the ventricle may have been due to inadequate mixing in the position of sampling in the auricle   The possibility of a small right to left ventricular shunt is suggested by the lowered arterial oxygen saturation
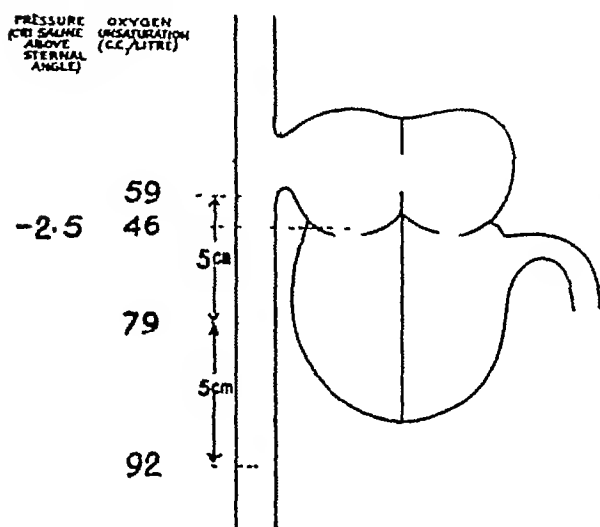
FIG 10 —Case 4   Data obtained by cardiac catheterization
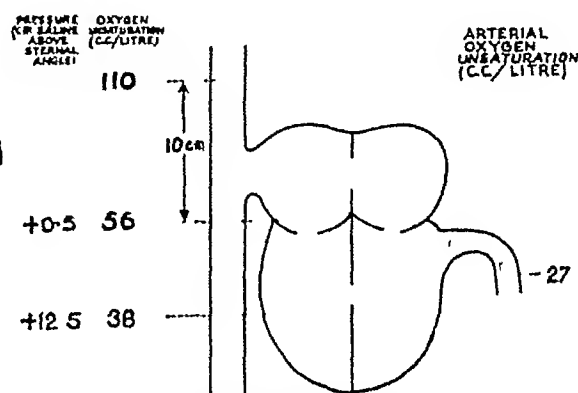
FIG 11 —Case 5   Data obtained by cardiac catheterization

Case 6   A woman, aged 26, had suffered from breathlessness and blueness of the lips on exertion for one year   There was no history of rheumatic fever   The jugular venous pressure was raised to 1 cm above sternal angle level, but the liver was not enlarged and there was no œdema   The blood pressure was 114/76   There was a harsh systolic murmur at the apex and the pulmonary second sound was accentuated   A cardiogram showed sinus rhythm, right axis shift, and depression of S–T in leads II and III   P II was 0 3 mv   A chest X-ray showed enlargement of the right ventricle, the conus and the pulmonary arteries, but no enlargement of the left auricle (Fig 13, see p 299)   The vital capacity was 2300 ml   She developed severe cardiac failure and cachexia with extreme peripheral cyanosis   Death occurred 18 months after the first admission to hospital

Post-mortem examination   The heart weighed 481 g and showed hypertrophy and dilatation of the right ventricle   The right auricle was dilated, but no septal defect was found The left ventricle and auricle were normal, and so were the valves   Atheroma of the pulmonary arteries with some recent thrombosis was found, and the small branches of the pulmonary artery showed great thickening of the arterial wall and reduction of the size of the lumen There was no pulmonary emphysema

Comment   The samples from the right ventricle and auricle showed no evidence of a left to right shunt (Fig 14)   Arterial saturation was originally normal though slightly reduced 8 months later when severe failure was present (Fig 15)   There was no evidence of right to left shunt or of chronic disease in the lungs   These findings with the demonstration of a greatly raised mean right ventricular pressure suggested a diagnosis of primary pulmonary hypertension   The post-mortem findings supported this view

Fig 13 —Case 6   Primary pulmonary hypertension

Fig 12 —Case 5   Patent interauricular septum
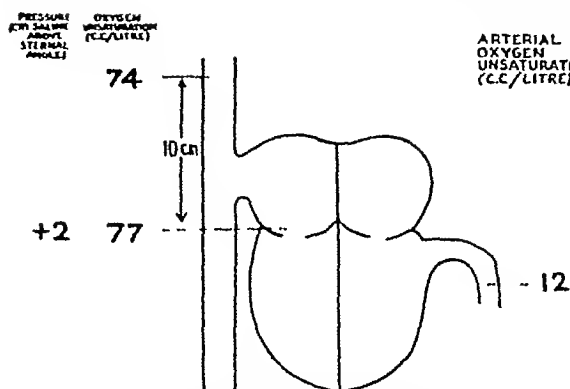
FIG 14 —Case 6   Initial data obtained by cardiac catheterization
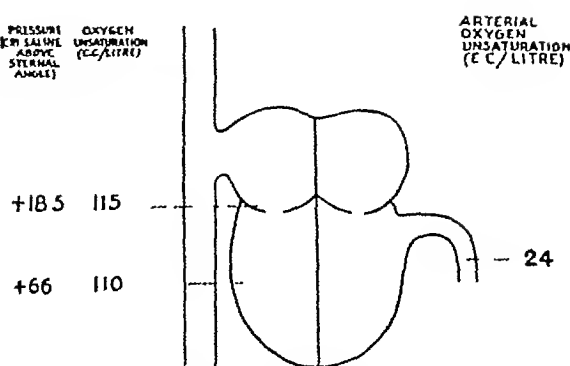
FIG 15 —Case 6   Data obtained 8 months later when severe failure was present

Case 7   A boy, aged 15, had been diagnosed at the age of 4 as a case of Fallot's tetralogy He was admitted to hospital following hæmoptysis   He was cyanosed, showed defective growth, and had clubbing of the fingers   The jugular venous pressure was not increased, the liver was not enlarged and there was no œdema   The blood pressure was 80/20, and the heart rate 96, the rhythm being regular   A harsh systolic murmur was heard, maximal in the third left interspace   A cardiogram showed sinus rhythm, right axis shift and depression of S–T III   Chest X-ray showed a classical " sabot " heart (Fig 18, see p 301)

Comment   The decrease in the saturation of arterial blood indicated a considerable shunt from right to left (Fig 16)   The difference between right auricular and ventricular blood suggests the possibility that there was also some mixing from the left to the right ventricle

Case 8   A girl, aged 8, was known to have had a congenital heart lesion since birth   In recent months she had become easily fatigued and after mild exertion the jugular venous pressure became elevated   On examination there was no clubbing or cyanosis   The jugular venous pressure was at the level of the sternal angle at rest and the liver was palpable   A systolic thrill and a harsh systolic murmur were present in the third left interspace, and the pulmonary second sound was accentuated   The blood pressure was 100/50   A cardiogram showed right preponderance   Chest X-ray showed enlargement of the pulmonary arteries and right ventricle (Fig 19, see p 301)
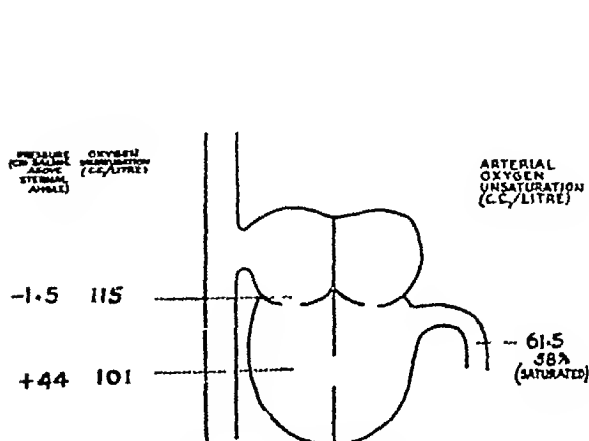
FIG 16 —Case 7   Data obtained by cardiac catheterization
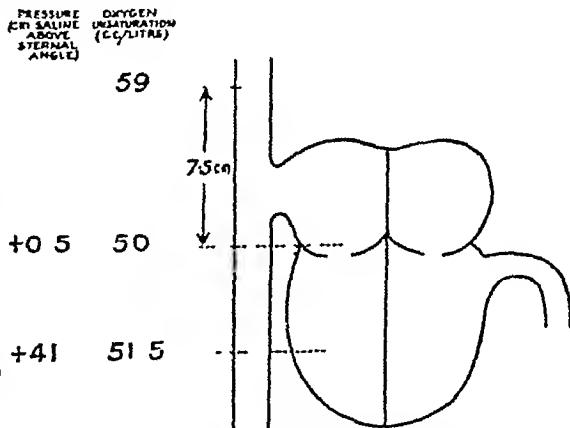
FIG 17 —Case 8   Data obtained by cardiac catheterization

Comment   In view of a pulse pressure of 50 mm Hg patent ductus was considered, while a left to right auricular shunt could not be excluded on clinical grounds   Catheterization

CARDIAC CATHETERIZATION

FIG 19—Case 8   Pulmonary stenosis

FIG 18—Case 7   Fallot s tetralogy

revealed no evidence of a shunt (Fig 17) Although an attempt to pass the catheter into the pulmonary artery failed, the greatly increased right ventricular pressure made a diagnosis of pulmonary stenosis almost certain

Case 9 A boy, aged 13, was known to have had cardiac murmurs since birth He played games at school and there was no history of cyanosis or excessive breathlessness The jugular venous pressure was not raised and there was no œdema The blood pressure was 90/40 and the heart rate was regular at 90 A thrill, a harsh systolic murmur, and a soft diastolic murmur were present in the pulmonary area, maximal in the second left interspace The pulmonary second sound was accentuated A diastolic murmur was present at the apex The hæmoglobin was 91 per cent A cardiogram was normal X-ray examination showed considerable enlargement of the right ventricle and the pulmonary arteries The left ventricle was also slightly enlarged There was no left auricular enlargement

Comment A case of patent ductus arteriosus (Fig 20) The mean pulmonary arterial pressure was surprisingly high, in view of the systemic blood pressure Considerable increase in right ventricular work from this high pressure may have resulted in hypertrophy comparable with the left ventricular hypertrophy from increased output, since the cardiogram shows no axis deviation
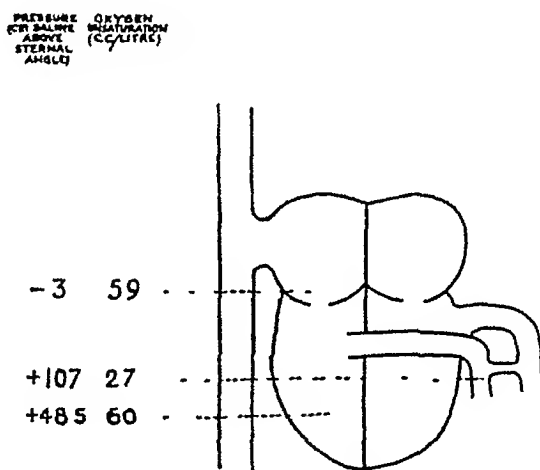
FIG 20

DISCUSSION

The precise diagnosis during life of congenital heart lesions has now more than an academic interest Ligation of a patent ductus arteriosus is a well-established method of treatment, while the procedures of Blalock and Taussig (1945) in Fallot's tetralogy seem very promising Even if the presence of a patent ductus is obvious, it may be of value to know whether other lesions are present or absent when considering ligation Enlargement of the pulmonary arteries, as a main finding, has long presented a difficult differential diagnostic problem for clinicians and radiologists Patent interauricular septum, mitral stenosis, pulmonary stenosis, Eisenmenger's complex, patent ductus arteriosus, cor pulmonale from emphysema, primary pulmonary hypertension and rupture of a syphilitic aorta into the pulmonary artery are among the conditions that may have to be considered Investigation of the right heart by catheterization may provide the answer, or at least further data on which a firmer diagnosis may be based

The conditions under which a left to right auricular shunt is reversed remain obscure Like Brannon, Weens, and Warren, we have tried various procedures such as the Valsalva experiment and different postures without producing any change in the arterial oxygen saturation. The intrathoracic pressure rises steeply during a Valsalva, and all chambers of the heart may be affected equally When the mitral valve is stenosed, any procedure tending to raise the pressure in the right auricle may result in at least an equal rise in the left so that the shunt remains left to right Case 3 shows that mean pressure in the right auricle may be high and the shunt still left to right In Case 1, where the mitral valve was probably functionally normal, a high right auricular pressure produced by transfusion did not reverse the shunt

It is difficult to make an exact quantitative estimate of the proportion of blood shunted from the left to the right heart Brannon, Weens, and Warren estimated that in some cases of patent interauricular septum the output of the right ventricle might be as much as three times that of the left While the systemic blood flow may be estimated from vena caval samples, it is not so easy to get an exact estimate of the output of the right heart The inflowing stream of arterial blood from the left auricle makes it difficult to be certain that samples from the right heart are completely " mixed " This difficulty is illustrated in Case 5

The normal mean right ventricular pressure is from 10 to 15 cm of saline above the mean auricular pressure The high ventricular pressures recorded in Cases 6, 7, and 8 indicated increased resistance in either the outflow tract of the right ventricle or in the pulmonary arteries In congestive heart failure from any cause, mean right ventricular pressure may be increased This finding, therefore, is more significant of organic obstruction in the right outflow tract if right auricular pressure is normal

SUMMARY

Samples of blood from the right auricle and right ventricle may be obtained by cardiac catheterization in cases of suspected cardiac shunts Blood so obtained contains more oxygen than vena caval blood if the shunt is from left to right Right to left shunts may be detected by a reduced arterial oxygen saturation in the presence of normally functioning lungs

Two of the five cases with patent interauricular septum showed a conspicuous increase in right auricular pressure with the shunt still left to right

A case with enlarged pulmonary arteries and a normal arterial oxygen saturation showed no evidence of a shunt and a greatly increased mean right ventricular pressure A diagnosis of pulmonary hypertension was confirmed post-mortem

A case of Fallot's tetralogy showed an increased mean right ventricular pressure The data suggested some left to right mixture of blood although the main shunt was from right to left

A child with enlarged pulmonary arteries showed no evidence of a shunt Mean right ventricular pressure was greatly increased and a diagnosis of pulmonary stenosis was made

A case of patent ductus arteriosus showed a greatly raised mean pulmonary arterial pressure, a considerably raised right ventricular pressure, and highly oxygenated pulmonary arterial blood samples

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2D

PROCEEDINGS OF THE BRITISH CARDIAC SOCIETY

The ELEVENTH ANNUAL GENERAL MEETING of the British Cardiac Society was held at Guy's Hospital, London, on Tuesday, May 6, 1947 Chairman MAURICE CAMPBELL The Chairman took the chair at 9 30 a m , 62 members and 19 visitors were present

PRIVATE BUSINESS

1 The minutes of the last meeting having been printed in the Journal (8, 233, 1946) were approved and signed
2 The Secretary reported that a balance of £8 16s 8d had been handed over at the transfer of the Secretaryship and said that subscriptions amounting to £78 were due in 1947–48   It was decided that the subscription should be increased to 20s for Ordinary members and 10s for Associate members
3 Boyd Campbell (Belfast) and McMichael (London) were elected members of the Council for the years 1947–51
4 The following new members were elected

Ordinary Members	Associate Members	
Wyn Jones	D Rhodes Allison	R W Luxton
Lovibond	Roland E Anderson	Wilfred Oliver
Sharpey-Schafer	Ronald Hartley	R Kemball Price
Suzman	Ronald Jones	Richard Turner
Swan	Geoffrey Konstam	

   Five Associate members were re-elected for a further period of three years
5 The following changes in the Rules were carried, *nem con* , on the recommendation of the Council
   Rule 8 Substitute " Rules 12 and 22 " for " Rule 12 "
   Rule 17 Add at the end " and shall take over office from his predecessor at the start of the meeting "
   Rule 21 Insert before " the Chairman-Elect ", " the Chairman "
6 The Secretary reported that as a result of representations to the President of the Royal College of Physicians, a Committee on Cardiology had been constituted by the College   The Report of this committee, dealing with the training of specialists in cardiology, the practice and teaching of cardiology, and the planning of cardiac services under the National Health Scheme, had been published and copies were available   The Secretary also announced the progress of arrangements for the International Conference of Physicians at which the Section of Cardiology would be under the Chairmanship of Sir Maurice Cassidy
7 The Council of the Society was authorized to decide on the election of new Honorary Members after the conclusion of the International Conference of Physicians
8 The Surgical Treatment of Hypertension was chosen as the main discussion at next year's meeting

DISCUSSION ON CARDIAC EMERGENCIES

(1) ACUTE RIGHT AND LEFT HEART FAILURE opened by BRAMWELL and McMICHAEL
(2) CARDIAC INFARCTION opened by BOYD CAMPBELL and HILL
(3) LOSS OF CONSCIOUSNESS opened by MAURICE CAMPBELL and LENDRUM
(4) PULMONARY EMBOLISM opened by PAUL WOOD

CRIGHTON BRAMWELL said that the two most important precipitating causes of *acute heart failure* were coronary occlusion and pulmonary embolism, both of which would be dealt with by later speakers   He also mentioned the possibility of rupture of a cusp of the

aortic valve and of sudden occlusion of the mitral orifice by a ball thrombus in the auricle He then referred to two causes of acute heart failure that had received less general recognition Sudden failure of the left auricle in association with severe mitral stenosis might occur unexpectedly, and he had reported two cases seen during pregnancy Secondly acute heart failure due to vitamin B_1 deficiency, though rare in this country was important since the treatment was specific and lesser degrees of vitamin deficiency might be a contributing factor in the production of heart failure

J McMICHAEL divided his remarks into acute left and acute right heart failure

Acute Left Heart Failure Opportunities had occurred of observing attacks of acute orthopnœa with the cardiac catheter in situ The arterial pressure rose above the previous level even in hypertensive subjects The right auricular pressure invariably rose in the attack and, as the lungs became congested, presumably the left auricular pressure also rose considerably Blood returning to the right heart contained less oxygen than before the attack, but owing to the increased oxygen uptake resulting from the struggle for breath the cardiac output was found to be slightly increased

In *treatment* the most effective and reliable remedy seemed to be *morphine,* under the influence of which right auricular pressure, metabolic rate, and arterial pressure fell It was not yet possible to say what was the exact sequence of events either in the precipitation of the attack or in the mechanism of its relief After morphine the next most reliable remedy was *theophylline-ethylene-diamine* which often reduced the right auricular pressure within 5 minutes *Venesection* should also be recognized as a most effective, though less convenient, measure *Intravenous digoxin* may not be satisfactory in these acute seizures An attack had actually been observed to come on following intravenous digoxin and perhaps precipitated by the pressor action of this drug on the arterial system

Acute Right Heart Failure The most striking instances occur in acute pulmonary embolism This subject is dealt with by Paul Wood Patients with emphysema heart, however, are liable to develop attacks of congestive failure during acute exacerbations of bronchitis In these attacks the cardiac output is high and the raised venous pressure should be regarded as to some extent a compensating mechanism Reduction of venous pressure by venesection or digoxin often brings down the cardiac output, and these measures are thus of little benefit as a rule (*Clin Sci*, 1947, 6, 187) The best treatment at this stage is an oxygen tent to improve the oxygen content of the blood, and measures to overcome the infection

S B BOYD CAMPBELL discussed the possible ætiology of *coronary infarction* Case histories of 169 hospital and 100 private patients were investigated Age groups, occupation, fat consumption, and previous infections were noted, 85 per cent of the private and 92 per cent of the hospital cases occurred in the 40 to 70 age group with 37 per cent and 31 per cent in the 50 to 59 group Over-indulgence of fatty foods has been prevented for many years by rationing and seems to have no bearing on the increase in infarction Occupation in both private and hospital cases showed similar findings No special occupation seemed to be associated with the occurrence of infarction Occupations found included civil servants, clergymen, clerks, farmers, skilled workmen, labourers, housewives etc Stress and strain seemed to have no bearing on the ætiology though the actual onset in some cases was associated with exertion and in others followed a heavy meal

It was difficult to find any definite infection in the history of previous illnesses Some cases had had some feverish illness within a few weeks of the infarction Case histories were of little help in solving the ætiology

He was indebted to J H Biggart, M G Nelson, and Florence McKeown for the lantern slides illustrating their recent work on coronary artery disease First slides were shown from

cases dying of acute rheumatism　The initial change was an acute arteritis affecting the media followed by intimal changes with healing fibrosis and then secondary degeneration The intimal fibrosis may almost occlude a large coronary artery　Similar changes were shown in coronary arteries of rabbits injected with horse serum　The final stages was demonstrated in a series of lantern slides of sections taken from the site of the coronary thrombosis　Intramural intimal hæmorrhage with fibrinoid degeneration preceded the thrombosis and was shown to be the precipitating factor　Secondary atheromatous changes were demonstrated While hypertension plays a part in initiating the intramural hæmorrhage there seems to be evidence that all the changes from the initial medial arteritis to the fibrinoid degeneration and intramural hæmorrhage are an allergic reaction in patients sensitized to some protein resulting from an infection or possibly ingested

J G W HILL spoke on the *electrocardiographic aspects of cardiac infarction*

MAURICE CAMPBELL said that even if *loss of consciousness* is rarely an emergency in the sense of needing urgent treatment, the anxiety caused and the difficulties of diagnosis justify its inclusion　The same word, syncope, is used for trivial fainting attacks and for a method of death and should, therefore, be banished from scientific discussion　It might be useful if it was recognized that syncope meant a sudden loss and fainting a gradual loss of consciousness, and he had sometimes used the terms in this sense　There is, however, no such agreement and it would at present be wrong because syncope is by definition (O E D) " a failure of the heart's action, resulting in loss of consciousness or sometimes in death "

A more accurate knowledge of attacks of unconsciousness will be difficult to acquire without more accurate descriptions and this should be helped by more precise definition of terms　The speed with which consciousness is lost seems one of the most fundamental distinctions, and I suggest that the word tachy-a-psychia should be used for the sudden loss of consciousness, seen in most Stokes-Adams attacks or in epilepsy, and brady-a-psychia for the gradual loss of consciousness seen in most fainting attacks in young people　Lipo-psychia is used most often by Hippocrates for swooning, but apsychia is an alternative that makes the compound words euphonious　I am indebted to Mr Yorke, Classical Tutor at New College, for coining these words for me

Loss of consciousness concerns the physiologist and neurologist even more than the cardiologist, but there is, perhaps, more knowledge of the provoking mechanism of unconsciousness in disorders of the heart than of the nervous system　The common factor in the former group is the production of cerebral anoxæmia—whether by changes of rhythm, including ventricular standstill as in many Stokes-Adams attacks, by standstill of the heart as in a few fainting attacks or during anæsthetics, by the combination of a slow heart and a fall of blood pressure or by one of these alone, as in most fainting attacks and in many cases of the carotid sinus syndrome, or by temporary arrest of the cerebral circulation by venous stasis or difficulty in auricular filling during violent spasms of coughing or after pulmonary embolism Anoxæmia without a change in the blood flow must also be remembered

Broadly speaking, these various cardiovascular causes—and there are many more—can be divided into those where there is arrest of the cerebral circulation, often but not necessarily with cardiac or ventricular standstill, and those where there is diminution of the cerebral circulation (as in the severe fall of blood pressure after a large cardiac infarct or with a very rapid paroxysmal tachycardia), this may reach a stage of deficiency severe enough to cause unconsciousness which will therefore generally be gradual

As a rule, therefore, tachyapsychia will mean sudden arrest of the cerebral circulation and bradyapsychia a gradual diminution of the cerebral circulation　there are, however, exceptions and, of course, many cases of tachyapsychia will be cerebral in origin　Arrest of the circulation

has greater dangers of the heart failing to start again and so tachyapsychia often has a much graver prognosis than bradyapsychia

Generally, however, a patient who has been unconscious can give the physician no direct indication as to whether the cause was cardiac or cerebral and the decision may be very difficult and may call for much knowledge and experience the symptoms produced in either way may be almost identical It is, in particular, essential to be on familiar terms with epilepsy, idiopathic or symptomatic, in both its major and minor forms,

The duration of the attack is of great importance in this connection A short attack, and this means one of not much more than two minutes, may be either cardiac or cerebral in origin A long loss of consciousness, and this means one lasting more than 5 or 10 minutes must be wholly or partly cerebral—partly, when a short cardiac arrest started the loss and produced changes in the cerebral cortex that prolonged the unconsciousness

I shall make some rather dogmatic statements that will help to clarify the discussion Arrest of the cerebral circulation for from 5–10 seconds by a pressure cuff round the neck (Rossen, Kabat, and Anderson, *Arch Neurol Psychiat*, 1943, **50**, 510) causes sudden loss of consciousness Standstill of the heart or of the ventricle for from 5–10 seconds also causes sudden loss of consciousness, so this is further evidence that both act in the same way by producing sudden arrest of the cerebral circulation

In unconsciousness due to cerebral anæmia, spasmodic movements or fits are dependent on the depth and duration of unconsciousness and not on its cause, and may, therefore, occur in attacks of all sorts They follow 15–20 seconds after the arrest of the circulation

Arrest of the cerebral circulation for 2 minutes in experiments on men or arrest of the circulation for 2 minutes by standstill of the heart in disease or during anæsthetics is compatible with perfect recovery

Standstill of the heart for 5 minutes is generally permanent, i e the patient is dead In the rare cases where the heart starts again after a longer interval than this, anoxæmia will have caused irreversible damage to the brain, especially to the cortex The first sign of this cerebral damage will often be a much longer period of unconsciousness Where the cerebral arteries are diseased as in many cardiac cases and most Stokes-Adams attacks a shorter period than 5 minutes may produce cerebral damage from which it is not possible to make a recovery

Standstill of the heart for some time more than 2 minutes but less than 5 minutes will produce cerebral damage from which it may be possible to make a perfect recovery The first sign of this cerebral damage may be a more prolonged period of unconsciousness This means that even in a case known to be cardiac and known to be unconscious for many minutes, it is of great prognostic significance to know when the circulation returns, i e when the heart starts beating Ultimately this period of between 2 and 5 minutes may be defined more precisely though there will always be great danger about recovery in such cases In clinical records of heart standstill periods of from 20 to 80 seconds are not often exceeded and these are well within the limits when complete recovery can take place

R G LENDRUM mentioned some of the conditions where a cardiac ætiology is wrongly and not infrequently diagnosed Cerebro-vascular epilepsy and even hypertensive crises can thus be mistaken, especially where the patient is already under care for cardiovascular disease Another is idiopathic epilepsy, if beginning in middle age, showing little or no movements and possibly having a prolonged sensory aura Epilepsy of the chronic alcoholic is aided in joining this group by wrong assessment of the cyanotic complexion

Patients who take attacks of hysterical hyperventilation with " unconsciousness " are looked on as liable to " heart attacks," this being most likely where the process starts with retrosternal discomfort (globus hystericus)

In nervous, hypersensitive people, consciousness of even a single ventricular extrasystole

gives rise to faintness and fear that consciousness will be lost   Actual appreciation of the feeling of " falling over to sleep " can occur   Here too a similar acute fear arises and in both cases the resulting tachycardia and palpitation may lead to diagnostic confusion

Faintness after great unaccustomed effort occurs in healthy people and the patient and even his doctor, may decide that the heart has been " strained "

Aerogastric bloquee gives discomfort in the chest, faintness, and a premonition of death This is most likely in someone already affected with cardiac disease and thus is all the more readily diagnosed as a " heart attack "

PAUL WOOD analysed twenty cases of massive *pulmonary embolism*   Of the clinical features special attention was directed to the frequency of substernal pain (12)   Detailed studies of the behaviour of the arterial and venous blood pressure were presented   The arterial pressure fell abruptly and profoundly, reaching its lowest level within a matter of minutes or hours, and thus differed from its behaviour in acute myocardial infarction   The four patients with the lowest pre-embolic blood pressures all died at the time of the profound fall, no others died   The venous blood pressure rose sharply in all but two cases   A graph based on daily readings showed that the maximum elevation occurred within the first 24 hours, and was followed by a steady decline towards normal which was reached in 3–7 days   Maximum levels ranged between 2 and 10 cm above the sternal angle

The relationship of the venous blood pressure to the cardiac output was studied in one case When the venous pressure was lowered by means of cuffs on the thighs, the cardiac output fell   When the cuffs were removed the venous pressure and the cardiac output rose   It was concluded that the raised venous pressure was beneficial and that the heart was not overloaded The right ventricular pressure in this case, measured by means of cardiac catheterization, was −+32 cm of saline above the sternal angle with the subject nearly horizontal

The rest of the communication dealt with the electrocardiographic diagnosis   The multiple chest lead pattern previously described by the author (*Brit Heart J* , 1939, **1**, 49, and 1941, **3**, 21) was further amplified   The changing pattern was attributed to transient right ventricular stress, and was met in other conditions besides massive pulmonary embolism

SHORT COMMUNICATIONS

CONSTRICTIVE PERICARDITIS
H COOKSON

Three cases were reported illustrating variations in the onset and in the course of chronic constrictive pericarditis   In the first, a man of 24, the onset was acute with pericardial effusion and six months later the full picture of chronic constrictive pericarditis had developed Pericardectomy was done one year after the onset, and was partially successful, ascites persisting, because of technical difficulties adequate resection was not possible   The second case, a woman of 22, had an insidious onset with shortness of breath, puffiness of the face and swelling of the legs, there was X-ray evidence of old pleurisy   While under observation ascites developed and there was recurrent bilateral dry pleurisy   Pericardectomy was done 16 months after the onset, result good   The third case, a girl of 16, had abdominal symptoms at the onset   Over a period of 33 months the spleen has gradually enlarged and now fills more than half the abdomen   Gross thickening of pleura on both sides, extensive calcification in the pericardium, short attacks of paroxysmal tachycardia (auricular)   The signs of pericardial constriction are moderate and because of this and because of the huge spleen, of which the cause is obscure, pericardectomy has not yet been undertaken

There was no bacteriological proof of tuberculosis in any of the three cases   Cardiograms were very similar, showing S–T depression and T inversion   In the operated cases pulmonary

shadows, presumably due to pleural thickening, diminished   Little change in cardiac outline occurred after pericardectomy, but the abnormalities of T and S–T diminished

CONTINUOUS RECORDING OF SYSTOLIC BLOOD PRESSURE DURING THE UNCONSCIOUSNESS OF SUDDEN ANOXIA
F LATHAM   (Introduced by W K Stewart)

A method of continuous systolic blood pressure recording as employed at the R A F Institute of Aviation Medicine has been described, and also its application to the study of the unconsciousness of sudden anoxia

The technique utilizes pulse waves passing under an arm cuff to actuate a solenoid valve which automatically maintains the pressure in the cuff at systolic blood pressure level   The pulse waves are detected by means of a photoelectric cell applied to the finger

During a preliminary series of experiments, subjects were exposed in the decompression chamber to simulated altitudes of 35,000–40,000 feet and continuous blood pressure records taken during the subsequent anoxia, which ensued when their oxygen was cut off   The subjects were given oxygen when they became unconscious and the duration of each anoxia run was between 30–90 seconds   Difficulty was encountered in some of the experiments owing to convulsions occurring prior to unconsciousness

In the four cases investigated at this stage there did not appear to be any evidence of cardiovascular collapse and the blood pressure remained elevated throughout

A CASE OF LONG-STANDING AURICULAR FIBRILLATION
BY CRIGHTON BRAMWELL   To be published in full

FAMILIAL CARDIOMEGALY
BY WILLIAM EVANS   To be published in full

PERIPHERAL AND CENTRAL VENOUS PRESSURES IN TRICUSPID INCOMPETENCE
BY E P SHARPEY-SCHAFER   To be published in full

RIGHT AURICULAR DILATATION WITHOUT VALVE DISEASE

J L LOVIBOND described the case of a man of 28 who for the past 4 years had suffered from symptoms of chronic right heart failure with swelling of the neck, abdomen, and legs   An intracardiac thrombus was diagnosed during life but the underlying pathology was not revealed until necropsy   There was no history of rheumatic or other infection but, at the age of 14, his heart had been questioned because of cyanosis on swimming   At 21 tonsillectomy was performed for sore throats   At 24 his abdomen began to swell and he was found to have ascites, a big liver and spleen, radiological enlargement of the right auricle and superior vena cava, and auricular fibrillation   Failure was treated appropriately and normal rhythm restored by quinidine   From now on he became increasingly short-winded and ascitic, requiring regular abdominal paracenteses   For most of the next 4 years he remained in hospital   At 26 he had a lung infarct and later in the year underwent omentopexy without relief   At 27 venous pulsation in the neck and a striking apical triple rhythm were noted, but no murmurs   There was sinus rhythm with wide, bifid P waves in leads II and III and right axis deviation   There was no response to diuretics and his abdomen now required fortnightly tapping   Although a few months later he reverted to fibrillation and also suffered a further lung infarct his general condition continued to be well maintained   The absence of clinical evidence of tricuspid or other valvular disease and the exclusion of cardiac tamponade by aspirations of a small pericardial effusion without beneficial effect, together with the history of lung infarcts and the radiological finding of a dense inert shadow in the position of the right auricular appendix, prompted the diagnosis of right auricular thrombus   In the face

of constant requests for surgical relief from the patient, an intelligent salesman, operation was eventually agreed to and an adherent laminated thrombus (6 2×5 0×1 2 cm) was removed from a tensely dilated right auricle   Death occurred a few minutes later from pulmonary embolus   The heart (500 g) showed great dilatation and hypertrophy of the right auricle and moderate hypertrophy of the left, but the ventricles, valves, aorta, coronary and pulmonary arteries were normal   Microscopically there was diffuse myocardial fibrosis with great muscle hypertrophy and focal endocardial thickening of both auricles and, to a lesser degree, both ventricles   The liver (1485 g) and spleen showed " sugar icing " capsular thickening with advanced congestive reticular fibrosis of chronic back pressure   The pericardium and peritoneum were unaffected, and the lungs normal apart from old and recent infarcts   The condition was regarded as a healed generalized myocarditis of unknown origin, affecting the whole heart but principally the right auricle, causing its inordinate dilatation with resulting back pressure effects   The resemblance of the cardiac pathology to Fiedler's isolated myocarditis and to cases described by Kugel (1939), Levy and von Glahn (1944) and Bedford and Konstam (1946) were briefly discussed   A second case was shown of aneurysmal right auricle with fibrosis and focal stretching of its wall, due to thrombotic occlusion of the right auricular branches of the coronary artery

A New Sign in Coarctation of the Aorta

S Suzman demonstrated a new sign in coarctation of the aorta by means of which the superficial collateral arteries of the back and sides of the chest are caused to become visible when not visible previously, or to become much more prominent   The sign is best produced by causing the patient to stoop or bend forward and with the arms hanging down vertically An equally good method is for the patient to lie prone on a couch with a pillow under the chest and the arms hanging down over the edge of the couch   A good light is advantageous The explanation for this phenomenon is that there is partial compression and obstruction (in cases where the sign is positive) of the subclavian artery in the costo-clavicular space, and any change of posture that widens this space will thus release pressure on the subclavian artery and so cause a sudden filling up of superficial arteries so that they suddenly appear in places where none were visible before or become more prominent

In three cases out of four so tested, the sign was positive (subsequently three more cases tested showed this sign)   He suggested that this sign should be looked for as a routine in all cases of suspected coarctation of the aorta and in fact all cases of high blood pressure, for by this means there might be less likelihood of missing a superficial collateral circulation

The Retinal Vessels in Hypertension

By A Leatham   (Introduced by William Evans)   To be published in full

Partial Superior Vena Caval Block

By Sheila Howarth   (Introduced by Sharpey-Schafer)   To be published in full

Mass Thrombus of the Left Auricle

By R Benson   (Introduced by William Evans)   To be published in full

Lone Auricular Fibrillation

By S Prichard   (Introduced by William Evans)   To be published in full

PROCEEDINGS OF
THE INTERNATIONAL CONFERENCE OF PHYSICIANS

PRESIDENT THE LORD MORAN, M C , M D , P R C P

SECTION OF CARDIOLOGY

PRESIDENT ⁚ SIR MAURICE CASSIDY, K C V O , C B , M D , F R C P

The INTERNATIONAL CONFERENCE OF PHYSICIANS was held in London from September 8th to September 12th The five sessions of the Section of Cardiology were attended by four or five hundred cardiologists among whom were welcomed many distinguished visitors from overseas Two of the sessions were joint meetings with the Sections of Pædiatrics and of Disorders of the Chest, respectively The programme arranged was as follows

Sept 9th Joint Meeting of Sections of Cardiology and Pædiatrics Discussion on THE SURGERY OF CONGENITAL HEART DISEASE

   Morning Diagnosis and Treatment of the Cyanotic Group
      Dr Helen Taussig (U S A)
      Dr Alfred Blalock (U S A)
      Dr James W Brown (Great Britain)
      Contributions to the discussion were made by Prof C Laubry, Prof J McMichael, and Dr F N Wilson

   Afternoon The Surgery of Patent Ductus Arteriosus and of Coarctation
      Dr C Crafoord (Sweden)
      Dr Rae Gilchrist (Great Britain)
      Mr Holmes Sellors (Great Britain)
      Mr O S Tubbs (Great Britain)
      Dr G Biörck, Prof C Bramwell, Mr Price Thomas, Dr M Campbell, Dr S Suzman, and Dr I Lindgren also spoke

Sept 10th Morning Joint Meeting with Section of Chest Diseases Discussion on PULMONARY HEART FAILURE ACUTE AND CHRONIC

      Prof J McMichael (Great Britain)
      Dr J Lenegre (France)
      Dr W D W Brooks (Great Britain)
      Dr Paul Wood (Great Britain)
      The following members also spoke Dr C Lian, Dr F N Wilson, Dr Fletcher, Dr Hammarström, and Dr G Biörck

   Afternoon Discussion on THE CLINICAL VALUE OF CHEST LEADS
      Dr F N Wilson (U S A)
      Dr C W Curtiss Bain (Great Britain)
      Dr Terence East (Great Britain)
      Contributions were also made by Dr I G W Hill, Prof C Lian, and Dr Van Dooren

Sept 11th   Discussion on The Use of the Phonocardiogram in Clinical Cardiology

Dr William Evans (Great Britain)
Dr C Lian (France)
M Minot (France)
Prof C Bramwell and Dr Evan Bedford also spoke

Sept 12th   Communications

1 The Septal Anastamoses of the Coronary Arteries
Prof C Laubry (France)
Dr Evan Bedford also spoke

2 Repetitive Paroxsysmal Tachycardia
Dr John Parkinson and Dr C Papp (Great Britain)
Contributions to the discussion were made by Dr F N Wilson, Dr C Lian,
    Dr Lenègre, and Prof C Laubry

3 *Sympathectomy for Hypertension* preliminary experiences
Dr Geoffrey Bourne (Great Britain)
Mr E G Tuckwell (Great Britain)
Dr F N Wilson and Dr Hammarstrom contributed to the discussion

4 Tomography in the study of Cardiovascular Disease
Dr E Tiscenco (Great Britain)
Dr J H Wright (Great Britain)

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